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BISMUTH IN THE TREATMENT OF SYPHILIS

REPORT OF CLINICAL AND EXPERIMENTAL STUDIES *

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PHILADELPHIA

It appears that Balzer was the first to suggest bismuth as an antisyphilitic drug in the treatment of human syphilis. Anticipating such an employment of bismuth, Balzer [1] first studied its effects in dogs. Severe untoward reactions consisting notably of stomatitis and enteritis resulted in the animals treated, and Balzer discontinued his studies.

In 1916, Sauton and Robert,[2] following the publication of their work on the bactericidal action of bismuth compounds, reported on the spirocheticidal action of bismuth in hen spirillosis due to *Spirochaeta gallinarum*. The drug they employed was sodium tartrobismuthate. Their anticipated work on the action of bismuth in the treatment of recurrent fever and of syphilis was interrupted by the recent war.

Sazerac and Levaditi, in 1921 [3] and 1922,[4] reported the results of their experiments on bismuth compounds—bismuth ammonium citrate, lactate, subgallate, oxyiodgallate, and sodium and potassium tartrobismuthate, in the treatment of rabbit syphilis. They observed that these salts of bismuth possessed a spirocheticidal action. The least toxic and most effective was sodium and potassium tartrobismuthate which they proposed for treating human syphilis and were the first to employ, using it in an oil suspension by intramuscular injections.

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* From the department of dermatology and syphilology, clinic of Dr. J. F. Schamberg, Graduate School, University of Pennsylvania, and from the Research Institute of Cutaneous Medicine.

1. Balzer, M. F.: Expérience sur la toxicité du bismuth, Compt. rend. Soc. de biol. **41**:537, 1889.

2. Robert, A. E., and Sauton, B.: Action du bismuth sur la spirillose des poules, Ann. de l'Inst. Pasteur **30**:261, 1916.

3. Sazerac, R., and Levaditi, C.: Compt. rend. Acad. d. sc. **172**:1391, 1920; **173**:338, 1921.

4. Sazerac, R., and Levaditi, C.: Étude de l'action therapeutique du bismuth sur la syphilis, Ann. de l'Inst. Pasteur **36**:1 (Jan.) 1922. Levaditi, C.: Le bismuth dans la syphilis, Presse méd. **59**:633 (July 26) 1922.

Subsequent to this study they reported [5] equally favorable results in the treatment of rabbit syphilis with precipitated bismuth as with sodium and potassium tartrobismuthate. The compound was injected in oil suspension.

As a result of the elaborate researches of Sazerac and Levaditi, the clinical use of bismuth as an antisyphilitic drug has been made possible. The favorable results reported by them in the treatment of human syphilis with sodium and potassium tartrobismuthate were confirmed first by Fournier and Guénot,[6] who reported on its employment in the treatment of 200 syphilitic patients in different stages of the disease. Other reports, mostly French, have since appeared, until now a considerable number of syphilitic patients in all stages of the disease with diverse manifestations have been reported treated with the drug. In most of these reports, sodium and potassium tartrobismuthate in an aqueous solution and an oil suspension of the same drug were used. Exceptions to this, however, are the reports of Fournier and Guénot [7] on the use of the metal bismuth (precipitated bismuth in isotonic solution) by intramuscular injections; Lacapere and Galliot [8] on the intravenous injections of colloidal suspension of bismuth; Grenet, Drouin and Richon [9] on the intravenous injections of an aromatic bismuth compound—a sodium derivative of trioxybismuthobenzoic acid; Horta and Ganns [10] on the intramuscular injections of sodium tartrobismuthate and Azoulay [11] on the intramuscular injections of quininbismuth iodid and also bismuth citrate.

The foregoing reports show that bismuth is therapeutically active when employed in the treatment of human syphilis.

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5. Sazerac, R., and Levaditi, C.: Action du bismuth en tant que corps simple sur la syphilis, Compt. rend. Soc. de biol. **86**:817, 1922.

6. Fournier, L., and Guénot, L.: Traitement de la syphilis par le bismuth, Bull. Soc. franç. de dermat. et syph., No. 9, 425, 1921; Ann. de l'Inst. Pasteur **36**:14 (Jan.) 1922.

7. Fournier, L., and Guénot, L.: Action therapeutique du bismuth, en tant que corps simple, dans la syphilis humaine, Compt. rend. Soc. de biol. **86**:908, 1922.

8. Lacapere and Galliot: Presentation d'un composé bismuthique injectable dans les veines. Premiers resultats, Bull. Soc. franç. de dermat. et syph., No. 5, 210-214, 1922.

9. Grenet, H.; Drouin, H., and Richon, L.: An Aromatic Bismuth Compound in the Treatment of Syphilis, Bull. de l'Acad. de méd. **87**:658, 1922.

10. Horta, P. deF., and Ganns, Paulo: A New Spirillicidal Salt of Bismuth. Its Action in Syphilis and Other Cutaneous Affections (Preliminary Note), Brazil-med. **36**:81, 1922.

11. Azoulay, R.: A Case of Malignant Syphilis Treated by Quinin Iodobismuthate, Bull. Soc. franç. de dermat. et syph., No. 2, 57, 1922; Bismuth Stomatitis, Presse méd. **30**:134, 1922.

This report is based on an experimental study of bismuth as a spirocheticidal drug in rabbit syphilis, which determined the ratio between the therapeutic active dose and the lethal dose;[12] it also presented the clinical results from the use of bismuth in the treatment of fifty syphilitic patients in the three stages of syphilis, the majority of whom presented a cutaneous manifestation of the disease. The bismuth preparations employed in this study were the French preparations of sodium and potassium tartrobismuthate in aqueous solution and in olive oil; potassium tartrobismuthate (see chemistry of bismuth compounds) prepared by Dr. George W. Raiziss and bismuth trioxid employed in olive oil and by inunctions.

THE CHEMISTRY OF BISMUTH COMPOUNDS

Although the structural formula of bismuth tartrate has not as yet been definitely established, several alkali salts of this compound have been prepared and designated either as bismuthotartrates or tartrobismuthates. In this study we have selected the potassium salt because its chemical constitution is probably more definite, its preparation easier, and because its spirocheticidal action was regarded as efficient as that of "sodium and potassium tartrobismuthate," which is probably a mixture of the potassium and sodium salts. The sodium salt, on the other hand, was not studied on account of its instability.

According to Rosenheim and Vogelsang,[13] the constitution of potassium tartrobismuthate may be represented by the formula:

$$\begin{matrix} CH(OBiO).COOK \\ CH(OBiO).COO(BiO)\ 4H_2O \end{matrix}$$

and should contain 67.08 per cent. of bismuth; but the product prepared by Dr. George W. Raiziss and used in this study had a bismuth content of only 62 per cent. We have also analyzed several commercial samples of sodium and potassium tartrobismuthate and found less than 52 per cent. of bismuth. Bismuth trioxid, which should theoretically contain 89.6 per cent. of bismuth, was not analyzed.

THE CLINICAL USE OF BISMUTH IN THE TREATMENT OF SYPHILIS

All of the bismuth preparations which have been employed in the treatment of syphilis, with two exceptions mentioned in the foregoing —colloidal bismuth and a sodium derivative of trioxybismuthobenzoic acid—are administered intramuscularly. Intravenous administration is positively contraindicated, since the drug is toxic when injected in this

12. The histologic changes in rabbits succumbing to the lethal dose of the bismuth preparations employed are being studied in collaboration with Dr. Baldwin Lucke and will be reported separately.

13. Rosenheim, A., and Vogelsang, W.: Several Salts and Complex Salts of Bismuth, Ztschr. f. anorg. Chem. **48**:205, 1906.

manner in rabbits (see animal experimentation). Intramuscular injections are given in the same way as is mercury. Sodium and potassium tartrobismuthate is administered either in an aqueous solution or in an oil suspension, the former in doses of 0.1 gm. in 1 c.c. every other day or 0.2 gm. in 2 c.c. every fourth day. The oil suspension is usually administered in doses of 0.2 gm. in 2 c.c. of oil every fourth day. Stomatitis has been reported as occurring soon after a single dose of 0.5 gm. of sodium and potassium tartrobismuthate.

The bismuth preparations employed in this study were given in varying dosages at variable intervals. Sodium and potassium tartrobismuthate in aqueous solution and potassium tartrobismuthate in aqueous solution were administered in doses of 0.1 gm. in 1 c.c., triweekly or every other day, or 0.2 gm. in 2 c.c. for a limited number of injections, or 0.2 gm. was given in alternating doses with 0.1 gm. An oil suspension of sodium and potassium tartrobismuthate was given in 0.2 gm. doses every fourth day, and bismuth trioxid in olive oil in doses of 0.1 gm. in 1 c.c. of oil triweekly and 0.2 gm. in 2 c.c. every fourth day.

The different dosages of the bismuth preparations were administered in order that the patient should receive as much of the drug as is possible in a given time without developing an untoward reaction of bismuth, particularly stomatitis, which is one of the early toxic symptoms. It was observed that this amount of the drug is differently borne in different patients. The earliest appearing untoward reactions were noted after a total administration of 1 gm. of the aforementioned preparations in 0.1 gm. doses injected in the course of one month. This, however, is exceptional. On the other hand, untoward reactions in other cases were not noted until as much as a total of 2.5 gm. had been administered in divided doses in the course of one month.

The total amount of one or the other bismuth preparations that can be well tolerated in a specified time, say one month, cannot be stated arbitrarily. The majority of patients will perhaps tolerate about 2 gm. in one month without developing any untoward reactions.

Levaditi [13a] advises the following plan of treatment: An oil suspension of sodium and potassium tartrobismuthate in 0.2 gm. doses administered in 2 c.c. every three or four days until a total of 2.8 gm. to 3 gm. has been administered, followed by a rest period of one month, then a repetition of this treatment until the Wassermann test is maintained negative.

Fournier and Guénot [6] advise the use of an oil suspension of sodium and potassium tartrobismuthate given in the following manner:

13a. Levaditi, C.: Le bismuth dans la syphilis, Presse méd. **30**:633 (July 26) 1922.

one course of treatment consisting of ten to twelve injections in doses of 0.2 gm. to 0.3 gm. to be given in about one month.

In my experience, this plan of treatment is too intensive, as it would produce stomatitis in many of the patients so treated. No definite plan of treatment was pursued in this study, as aforementioned, the dosage and interval of treatment being regulated by the conditions. After untoward reactions were noted the dosage was decreased. After the administration of a total of 2.5 gm. given in a period varying from one to two months, a rest period of about one month was instituted, followed by the administration of a total of another 2.5 gm. of the drug.

UNTOWARD REACTIONS OF BISMUTH THERAPY IN SYPHILIS

The early untoward reactions observed in this study were a foul breath [14] and a gingival blue line. The nature of the foul breath is such that when appearing after bismuth therapy there is little doubt as to its significance. This symptom was almost always associated with a blue line on the gums. In some patients, it preceded the blue line; and in others, the latter was present in the absence of the foul breath. The foul breath and the gingival blue line forecast the appearance of stomatitis and are associated with it.

The blue line, which is indistinguishable from that seen in plumbism, appears on the dental margin of the gums (Fig. 1). It usually appears first on the gingival margin of the incisor teeth, both anteriorly and posteriorly, and may later appear on the gingival margin of all the teeth. It is said to represent a precipitation of bismuth due to the action of hydrogen sulphid of the buccal cavity, which forms a bismuth sulphid. After its appearance, it persists if bismuth is continued and disappears after cessation of treatment. It was observed in this study that a well marked blue line disappears in about one month after treatment is stopped (Case 1).

Bluish spots on the gums, tongue and buccal mucous membrane may appear with the gingival blue line. They likewise represent a deposit of bismuth sulphid.

STOMATITIS

Bismuth stomatitis differs from the well-known picture of mercurial stomatitis in the lesser degree or absence of salivation, the presence of a diphtheroid membrane, a gingival blue line and bluish spots.

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14. It is interesting to note the following from Cushing's volume on Pharmacology, Ed. 5, page 693: "A symptom formerly noted in cases treated with bismuth was an extremely disagreeable odor in the breath, but this has been shown to be due to the presence of tellurium in the preparation." None of the bismuth preparations employed in this study contained tellurium.

The local lesions vary from a localized catarrhal gingivitis to ulcerations, which appear around the teeth and are usually covered by a false membrane. In the more advanced stage, there is a generalized ulcerative stomatitis which may be accompanied by ulcers involving the tongue and buccal mucosa.

The benign form of bismuth stomatitis soon disappears after bismuth treatment is discontinued, and is of little consequence. The severe forms with extensive ulceration are of greater import. Most of the cases of stomatitis reported have been of the benign form.

Milian and Perin [15] and Azoulay [11] have shown that infection with Vincent's spirochetes and its associated bacillus play an important rôle in the production of the ulcerative form of bismuth stomatitis.

The incidence of stomatitis is intimately associated with the intensity of bismuth treatment and the hygienic condition of the mouth of the patient treated. It is to be noted in most of the reports on the occurrence of bismuth stomatitis that the bismuth preparation was given in doses of 0.2 gm. and even 0.3 gm. repeated at frequent intervals for as many as ten to twenty consecutive injections.

Other untoward reactions are chills and fever occurring soon after an injection of bismuth. Loss of weight, anorexia and malaise may appear after prolonged treatment with bismuth. These symptoms were noted in a few of the patients in our series. The following reactions were not noted but have been reported by others: polyuria (Fournier and Guénot [6]) which disappears soon after the cessation of treatment and which is said to occur at times after the oral administration of bismuth. Milian [16] and Ducrey [17] report symptoms of enteritis occurring following bismuth therapy, and in others localized eczematous eruption, rubeoliform eruptions and discrete purpuric eruptions. All of the latter symptoms are apparently uncommon.

Only a few of the patients in this series developed albuminuria after bismuth therapy. From the report of others, albuminuria is apparently not a common occurrence after the administration of bismuth. However, severe nephritis has been reported. Although this is exceptional, nevertheless in the present state of our knowledge it is desirable to conduct frequent examinations of the urine of patients receiving bismuth treatment.

After the administration of bismuth a black deposit may form in the urine after standing, or it may be black at the time it is voided.

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15. Milian and Perin: Bismuth Stomatitis, Bull. et mém. Soc. méd. d. hôp. de Paris **38**:135, 1922.

16. Milian, G.: Bismuth Salts in Antisyphilitic Therapeutics, Paris méd. **12**:189, 1922.

17. Ducrey, C.: The Treatment of Syphilis with Bismuth, Policlinico **29**: 313, 1922.

This has been shown by Demelin [18] to be due to bismuth sulphid, which is formed by bacterial action in the urine on the bismuth excreted therein.

A foul breath and gingival blue line, which are prodromal symptoms, should be stressed as important "danger signals" so far as the further administration of bismuth is concerned. After their appearance, it is desirable to interrupt treatment temporarily; or, in lieu of this, to decrease the dose or increase the interval between treatment, not only to avoid the occurrence of stomatitis, which may be of the severe ulcerative type, but also to avoid a state of bismuth intoxication.

The presence or absence of these symptoms was taken by us as a criterion in determining the intensity and the duration of treatment by consecutive injections. After temporarily interrupting treatment, the latter was not resumed until the foul breath and gingival blue line disappeared. This occurred in three to four weeks. More significance attaches to the presence of the foul breath than to the blue line.

As already stated, the incidence of stomatitis is principally related to the intensity of bismuth treatment. Its occurrence has been regarded as an obstacle in the successful treatment of syphilis with bismuth.

Of the acute cases in this series, the active lesions of syphilis were entirely involuted, and in some the Wassermann test became negative before it was necessary to curtail or to stop treatment temporarily. In the treatment of patients with tertiary syphilis, when considerable and prolonged treatment is necessary, bismuth cannot be administered in too large amounts at too frequent intervals without a rest period. In this respect bismuth treatment does not compare with arsphenamin treatment.

It is known that relatively enormous doses of bismuth can be taken by mouth without producing signs of intoxication. This is probably due to the fact that little is absorbed by the digestive tract. Although at times following oral administration of large amounts of bismuth, signs of intoxication may occur, these signs also occur following absorption from wounds and when injected in the form of Beck's paste. Absorption is more rapid following the therapeutic use of bismuth by intramuscular injection. It is logical to believe that following this treatment any of the symptoms of bismuth poisoning with which we are familiar may appear. There is doubtless much to learn regarding the untoward reactions from the prolonged administration of bismuth by intramuscular injections. The bismuth therapy of syphilis is too

18. Demelin: The Treatment of Syphilis with Bismuth, These, Paris (Vanderperre edit.), 1922. This reference was not available, quoted from Levaditi, footnote 13a.

recent to have given us full information in this regard. It is a matter of considerable importance that one practicing bismuth therapy of syphilis should be cognizant of the symptoms of bismuth poisoning and to watch for the appearance of these symptoms. It is shown in this study that the administration of an arbitary amount of bismuth in a specified time is not always possible. In the bismuth therapy of syphilis, as in the treatment of any infectious disease, the fundamental principal in therapeutics, namely, the importance of treating the patient as well as the disease, should not be neglected.

CLINICAL RESULTS IN THE TREATMENT OF SYPHILIS WITH BISMUTH

The clinical results with sodium and potassium tartrobismuthate in aqueous solution and in oil suspension, potassium tartrobismuthate in aqueous solution and bismuth trioxid in olive oil, which were employed in this study, corroborated the favorable reports of others employing sodium and potassium tartrobismuthate in aqueous solution and in oil suspension.

These results may be summarized as follows: Lesions of primary, secondary and tertiary syphilis involving the skin and mucous membranes were involuted after a total administration of bismuth ranging in total amounts from 0.3 gm. to 1.5 gm. These results obtained with each of the three bismuth preparations employed are shown in Figures 2, 3 and 4 (Cases 2, 3, 4). Patients with visceral syphilis and neurosyphilis were not included in this study. Others, however, have reported favorable results in the treatment of such cases.

EFFECT ON THE WASSERMANN TEST [19]

The four plus Wassermann reaction of patients with early secondary syphilis, previously untreated, and in the late secondary stage became negative, in the majority of cases, following a total administration of about 2 gm. of one or the other of the bismuth preparations employed. A few patients, however, required 3 gm. or more of the bismuth preparation before the test became negative. Such an instance occurred in

19. The Wassermann tests employed in this study were performed in the laboratory of Dr. John A. Kolmer. The method employed was the new Kolmer modification of the Wassermann test (Am. J. Syphilis **6**:64, 74, 82, 1922) based on results of studies in the standardization of technic (series of papers published in the Am. J. Syphilis starting with vol. 3, No. 1, 1919) and employing a new antigen. This method possesses sensitiveness and specificity and other desirable features (Schamberg, J. F., and Klauder, J. V.: The Clinical Value of the Kolmer Modification of the Wassermann Test, Clin. North America **5**:667 (Nov.) 1922. The advantages of the quantitative feature of this new test is shown in Case 1.

the patient whose photograph is shown in Figure 3 (Case 3). The four plus reaction of primary syphilis became negative after a lesser amount of the drug, and was proportional to the duration of the chancre. The four plus Wassermann reaction of tertiary syphilis required varying amounts of bismuth treatment and cannot be stated arbitrarily. Many of the tertiary syphilitic patients in this study are still under treatment, sufficient time not having elapsed to state the outcome in all cases. However, in some of them the four plus Wassermann reaction became negative after treatment with each of the three bismuth preparations employed. The following case may be appropriately mentioned. A patient in the tertiary stage of syphilis, the duration of the infection unknown, previously untreated, presented a nodular syphilid of the face. After a total administration of 0.8 gm. of potassium tartrobismuthate injected in aqueous solution in doses of 0.1 gm. three times a week, the syphilitic lesion was involuted. The four plus Wassermann reaction became negative after a total administration of 3.4 gm. given in the course of four months. There were no untoward reactions during treatment. At the termination of treatment there were only a few inflammatory nodules at the site of injections.

To be sure, the patients treated in this series were not regarded as cured after the initial negative Wassermann and treatment was continued. It was, therefore, not determined how long the Wassermann test remained negative after the cessation of treatment. However, the patient whose photograph is shown in Figure 1 disobeyed instructions after receiving a total of 2.4 gm. of sodium and potassium tartrobismuthate (the initial negative Wassermann test was obtained after 1.3 gm.) and absented himself for two months. After this period the Wassermann test was four plus. In another patient with a secondary eruption of syphilis, the four plus Wassermann became negative after a total administration of 2.3 gm. of sodium and potassium tartrobismuthate. No further treatment was administered (the patient disobeyed instructions) until three months later, at which time the Wassermann reaction was four plus. In one of Levaditi's patients, who was in the primary stage of syphilis, treatment was stopped after the initial negative Wassermann reaction. Seven months later the reaction was still negative.

The reports of Milian,[16] Guibert,[20] Fournier and Guénot[21] show that bismuth caused involution of syphilitic lesions which had resisted

20. Guibert, M.: A Case Resistant to Arsenic and Mercury Yielding to Treatment with Bismuth, Ann. de dermat. et syph. **3**:126, 1922.

21. Fournier, L., and Guénot, L.: The Treatment of Syphilis with Bismuth Salts. Ann. de l'Inst. Pasteur **36**:14 (Jan.) 1922.

treatment with the arsphenamin and with mercury. These are the so-called "arsenic-fast" and "mercury-fast" cases.[22]

DELAYED ACTION OF BISMUTH

It was observed in this study and also reported by others that the antisyphilitic effect of bismuth continues for some time after the administration of the drug. Some of the patients with active syphilitic lesions after receiving about 0.3 gm. of one or the other bismuth preparations absented themselves for from three to five weeks. On their return, the syphilitic lesions were either involuted or almost involuted. In others, it was observed that a positive Wassermann reaction became negative during a rest period in treatment. This prolonged antisyphilitic action of bismuth can doubtless be explained by the delayed absorption of the drug when injected intramuscularly and its slow elimination from the body (see "Distribution and Elimination of Bismuth"). This applies particularly after an injection of oil suspensions of sodium and potassium tartrobismuthate, or of bismuth trioxid.

The patients in the series herein reported were, with few exceptions, previously untreated. It was, therefore, not determined whether bismuth therapy is efficacious in producing a negative Wassermann reaction in those patients whose reaction remains persistently positive in spite of considerable treatment with the arsphenamin—in other words, the so-called Wassermann-fast cases.

PAIN AFTER INTRAMUSCULAR INJECTIONS OF BISMUTH PREPARATIONS

The pain and local reaction following an injection of 1 c.c. containing 0.1 gm. of sodium and potassium tartrobismuthate in aqueous solution is variable. Some injections produce only slight discomfort and no induration, others produce considerable pain and inflammatory nodules.

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22. Patients are occasionally seen with active syphilitic lesions which remain unchanged after arsphenamin treatment, and other patients whose lesions resist treatment with mercury. In the former patients, the lesions may involute after changing the brand of arsphenamin to which they were resistant, that is, changing from arsphenamin to neo-arsphenamin and vice-versa; or, by treating with mercury. Syphilitic lesions which resist mercurial treatment are likely to involute after arsphenamin treatment. Syphilitic lesions are rarely resistant both to arsphenamin and mercurial treatment. These clinical observations have led to the assumption that Spirochaeta pallida may become arsenic-fast or mercury-fast or both. There is some evidence of this experimentally. The author produced an arsenic-resistant strain of Spirochaeta pallida in syphilitic rabbits by initial treatment with a small amount of arsphenamin, later transplanting from the animals thus treated to other animals, then treating these animals with a slightly larger amount of arsphenamin, and so on until the curative dose was reached. It was possible in this manner to exceed the amount of arsphenamin which is the therapeutic active dose in animals not so treated. (Work not as yet published.)

A few of the patients complained of pain only at night when lying in bed, and disturbance of sleep. Mention may be made of patients who received a total of forty injections with only an occasional painful injection and whose gluteal muscles at the end of this treatment contained two or three inflammatory nodules. In two patients, the pain following each of three injections was so severe that further treatment was refused. They, however, received 0.2 gm. in 2 c.c. at each injection. This amount nearly always produces pain and inflammatory nodes, so that its employment in consecutive injections is not practicable.

Injections of an aqueous solution of sodium and potassium tartrobismuthate were more painful than any of the other bismuth preparations employed. The pain following injections of this preparation has been cited as an obstacle to its employment.

Injections of an olive oil suspension of sodium and potassium tartrobismuthate are less likely to cause pain, and when it does occur is less than that produced by an aqueous solution of the same drug. Moreover, its administration in doses of 0.2 gm. in 2 c.c. of oil is practicable.

Potassium tartrobismuthate was injected with a local anesthetic butyn. The drug was injected in doses of 0.1 gm. in 1 c.c. which contained 5 minims of a 2 per cent. solution of butyn. Without the anesthetic, the drug produced considerable pain, which was most evident during the injection and continued for a short period. In some patients, the pain was considerable after an injection of 0.2 gm. in 2 c.c.

Injections of an olive oil suspension of bismuth trioxid in doses of 0.1 gm. in 1 c.c. and 0.2 gm. in 2 c.c. were not painful. Inflammatory nodules resulting from the injections were unusual. The employment of a local anesthetic with this preparation is not necessary.

The addition of 5 minims of a 2 per cent. solution of butyn to 1 c.c. of an aqueous solution of sodium and potassium tartrobismuthate would no doubt considerably lessen or eliminate the pain resulting from an injection of this drug.

DISTRIBUTION OF BISMUTH AND ITS ELIMINATION WHEN INJECTED INTRAMUSCULARLY

Experimental studies which have been conducted on dogs and other animals show that after the salts of bismuth are injected intramuscularly, bismuth is found in the liver, kidney, spleen, brain and salivary glands. It is eliminated in the urine, saliva, bile, feces and sweat. Radiographic examinations at the site of injection of bismuth show that it remains in the tissues for a long time after injection.

Aubry and Demelin[23] have perfected Leger's method of detecting bismuth. With their method, the metal can be detected in a dilution of 1:600,000. These investigators found bismuth in the blood and spinal

23. Aubry: Soc. de Pharm., Nov. 9th, 1921. This reference was not available, quoted from Levaditi 13.

fluid of patients who were being treated with sodium and potassium tartrobismuthate and studied its elimination in the aforementioned fluids. In the urine, bismuth appeared from eighteen to twenty hours after the drug was administered, and was detected from twenty to twenty-five days after a course of treatment consisting of a total administration of 2.0 to 2.5 gm. of tartrobismuthate of sodium and potassium.

BISMUTH INUNCTIONS

The spirocheticadal action of inunctions of bismuth trioxid observed in the treatment of syphilitic rabbits, and the fact that this method of bismuth administration has not, to my knowledge, been employed in the treatment of human syphilis, led to its employment in the treatment of syphilitic patients.

Fig. 1 (Case 1).—Blue line along dental margin of gums represents bismuth deposit (indistinguishable from the blue line of plumbism).

Finely pulverized bismuth trioxid was employed in amounts ranging from 0.5 to 2 gm. in a total of 4 gm. of hydrous wool fat and petrolatum. This ointment was used as an inunction and applied daily to patients presenting cutaneous lesions of syphilis. Bismuth administered in this manner exerted a feeble spirocheticidal action. A considerable number of inunctions were required to cause involution of the syphilitic lesion. Its antisyphilitic action was less apparent than the same action of mercury administered by inunctions.

REPORT OF CASES

Case 1 (Fig. 1).—A woman, aged 39, who had an asymptomatic infection, the duration of which was unknown, had received two injections of neo-arsphenamin, subsequent to which jaundice appeared. After the disappearance of jaundice,

bismuth therapy was instituted. The Wassermann reaction with 0.1 c.c. of serum was four plus; with 0.05 c.c., it was four plus; with 0.025 c.c., it was four plus; with 0.005 c.c., it was two plus; with 0.0025 c.c., it was negative. Triweekly intramuscular injections were given of 0.1 gm. in 1 c.c. of sodium and potassium tartrobismuthate in aqueous solution. After the seventeenth consecutive injection (1.7 gm. total), the Wassermann reaction with 0.1 c.c. of serum was four plus; with 0.05 c.c., it was four plus; with 0.025 c.c., it was one plus; with 0.005 c.c. and 0.0025 c.c. it was negative. After the twentieth consecutive injection (2 gm.), the initial reaction appeared, consisting of chill and fever. At this time, the breath was foul and the blue line was first discovered. Urinalysis and examination of the blood smear were negative. Treatment was suspended for five weeks, at which time only a trace of blue line remained, and the breath was no longer foul. Treatment with 0.1 gm. weekly was resumed. The Wassermann reaction at the end of the rest period with 0.1 c.c. of serum was four plus; with 0.05 c.c., it was three plus; with 0.025 c.c., it was one plus; the remaining dilutions were negative. The Wassermann test performed according to the foregoing method

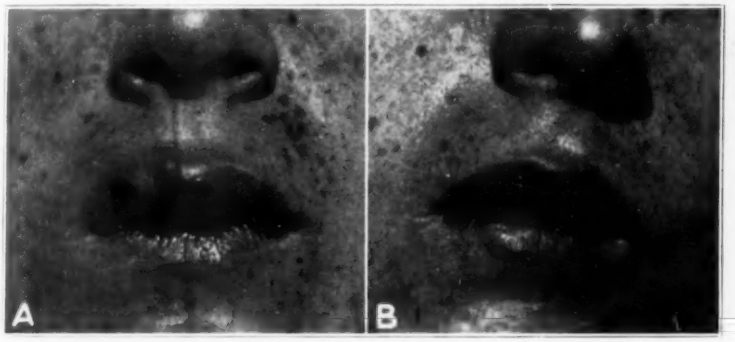
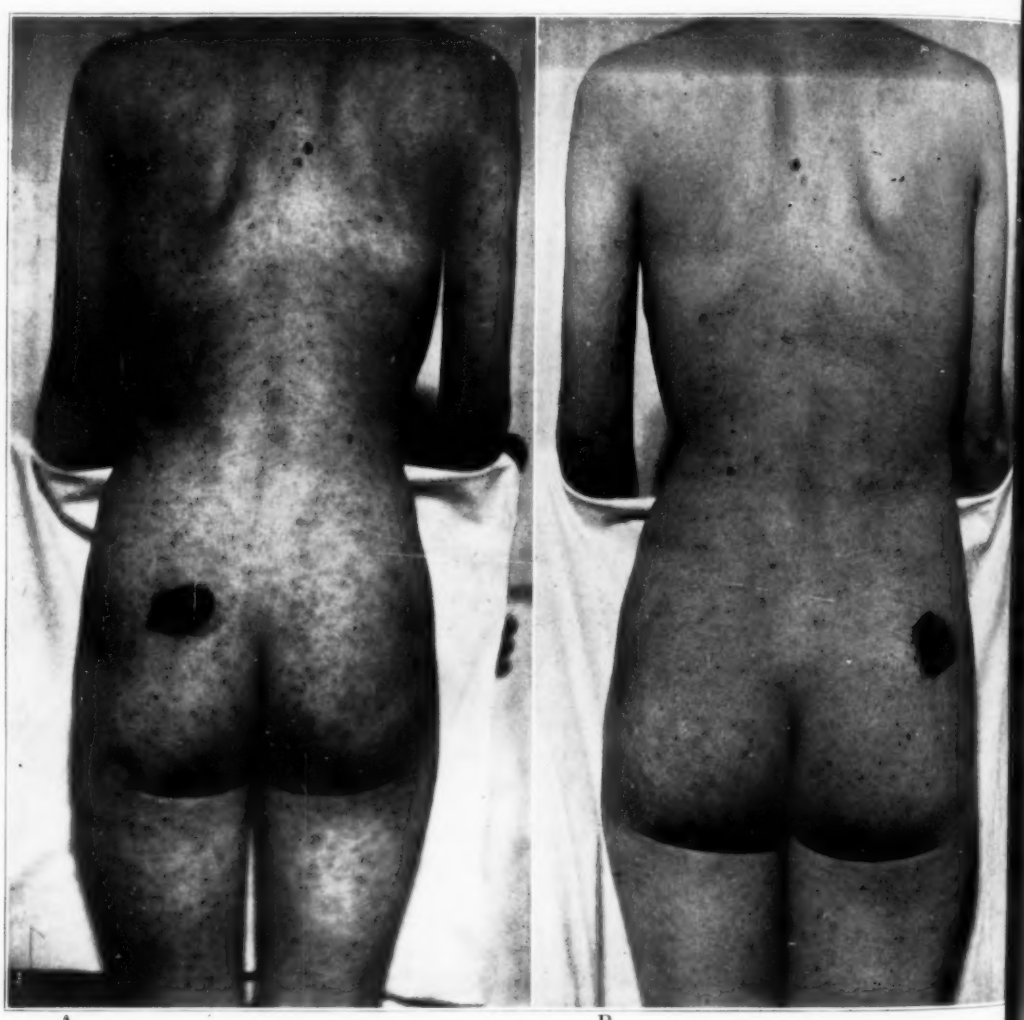


Fig. 2 (Case 2).—Multiple chancre of the lip; *A*, before treatment; *B*, after treatment.

showed about 50 per cent. improvement after a total administration of 2 gm. of the bismuth preparation, although the reaction with 0.1 c.c. remained four plus (Fig. 1).

Case 2 (Fig. 2).—There was considerable induration. The cervical glands were greatly enlarged (Fig. 2 *A*). The dark-field examination was positive; the Wassermann reaction with 0.1 c.c. of serum was four plus; with 0.05 c.c., it was four plus; with 0.025 c.c., it was three plus; with 0.005 c.c., and with 0.0025 c.c., it was negative. The patient was treated with sodium and potassium tartrobismuthate in aqueous solution, 0.1 gm. in 1 c.c. being administered intramuscularly, three times a week. Twenty hours after the initial injection, the dark-field examination was negative. After the fourth injection, induration of the chancre had entirely disappeared; the cervical glands were about one-half their former size. Both chancres had entirely healed (Fig. 2 *B*) after the ninth injection (0.9 gm., total). The Wassermann test was negative after the thirteenth injection (1.3 gm., total). After the nineteenth injection there was no apparent enlargement of the cervical glands, although they were palpably enlarged. Triweekly injections continued until

a total of 2.4 gm. had been administered. At this time the breath was not foul; the gums were in good condition. A rest period of one month was advised. The patient returned after two months, at which time the Wassermann reaction was positive in the same degree and same dilution of serum as before treatment. After a further administration of 1.8 gm. the Wassermann reaction again became negative.



A B

Fig. 3 (Case 3).—Generalized macular syphilid; *A*, before treatment; *B*, after treatment with potassium tartrobismuthate.

Case 3 (Fig. 3).—The duration of the eruption was one month. No chancre was demonstrable. The Wassermann test with 0.1 c.c. of serum was four plus; with 0.05 c.c., it was four plus; with 0.025 c.c., it was four plus; with 0.005 c.c., it was four plus; with 0.0025 c.c., it was negative. Treatment consisted of triweekly intramuscular injections. The dose at each injection varied from

0.1 to 0.2 gm. After a total administration of 0.4 gm., the macular lesions on the face disappeared. Figure 3 *B* shows the result after a total administration of 1.2 gm. The syphilitic eruption at this time was completely involuted, discolored areas only remained, as shown in the illustration. The large black areas represent the application of iodin at the site of an intramuscular injection of potassium tartrobismuthate. Consecutive triweekly injections were continued until a total of 3 gm. of the drug had been administered in the course of six weeks. At this time the Wassermann reaction was still four plus. After a further administration of 1.6 gm. the Wassermann reaction became negative.

CASE 4 (Fig. 4).—The patient had a vegetating tertiary syphilid which was treated with bismuth trioxid suspended in olive oil injected intramuscularly in doses of 0.1 and 0.2 gm. Treatment was given at irregular intervals owing to the irregular attendance of the patient. Figure 4 *B* shows the result after a total administration of 1.4 gm. given in ten injections in the course of two months. At this time, the lesion was completely involuted, pigmentation only remaining.

Fig. 4 (Case 4).—Vegetating tertiary syphilid; *A*, before treatment; *B*, after treatment.

It was apparent from these studies that little of the drug was absorbed when used in the form of inunctions. It is possible that greater absorption may occur with other bismuth preparations. Further studies are being conducted in which the metal bismuth, colloidal bismuth and other soluble bismuth preparations are being employed in the form of inunctions.

ANIMAL EXPERIMENTATION

In this study, twenty-five syphilitic rabbits were employed to determine the therapeutic active dose of sodium and potassium tartrobismuthate in aqueous solution and in an olive oil suspension; an aqueous solution of potassium tartrobismuthate and an olive oil suspension of

bismuth trioxid. Fifty normal rabbits were employed to determine the maximum tolerated and lethal doses of these drugs.

Intravenous injection of an aqueous solution of sodium and potassium tartrobismuthate and of potassium tartrobismuthate is toxic. The majority of rabbits injected intravenously with more than 0.005 gm. of either of these drugs per kilogram of weight did not survive.

The experiments to determine the therapeutic active dose of the bismuth preparations were conducted by intramuscular injections. The animals treated had well developed scrotal chancres, the serum from which disclosed many motile spirochetes under the dark-field microscope, or in lieu of a chancre there were many large nodes palpable in the

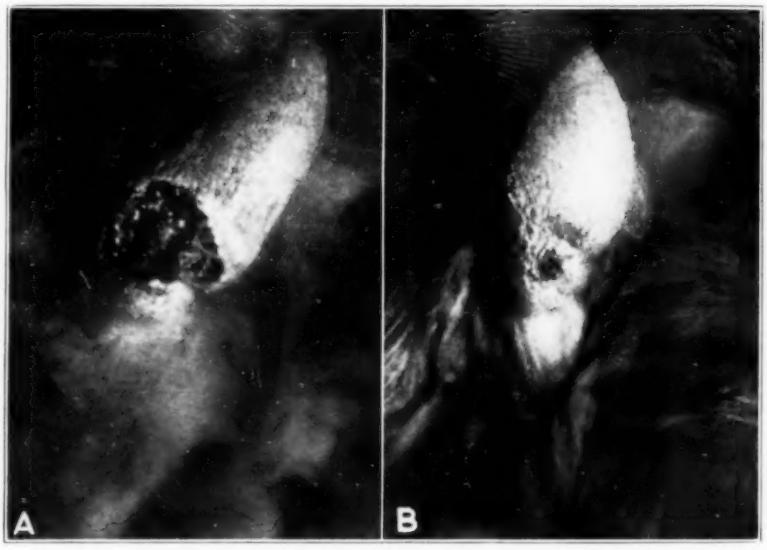


Fig. 5.—Experimental scrotal chancre in rabbit; *A*, before treatment with 0.006 gm. per kilogram of body weight of arsphenamin injected intravenously: *B*, after treatment.

testes, the serum obtained from puncturing these nodes containing many motile spirochetes in each microscopic field.

The results following the administration of the therapeutic active dose of arsphenamin, that is, 0.006 gm.[24] per kilogram of body weight injected intravenously in rabbits with active syphilitic testicular lesions, was taken as a standard in determining the therapeutic active dose of the bismuth preparations. These results (Fig. 5 shows the gross result) are: Before treatment the dark-field examination of the surface of the

24. The curative dose of arsphenamin is about 0.012 gm. per body weight injected intravenously.

chancre or, in its absence, of serum obtained from puncturing testicular nodes, showed many motile spirochetes in each microscopic field. Twenty-four hours after treatment the dark-field examination showed only a few slightly motile or nonmotile spirochetes and many agglutinated organisms in each field. Dark-field examinations on subsequent days were negative. Grossly, the chancre or the nodes were appreciably smaller the following twenty-four hours and gradually lessened in size until complete involution occurred within eight days. There was no recurrence of testicular or scrotal syphilitic lesions during the following two months.[25]

It was determined that the therapeutic active dose of sodium and potassium tartrobismuthate in aqueous solution and in olive oil and potassium tartrobismuthate in aqueous solution was at least 0.05 gm. per kilogram of body weight; it was 0.15 gm. per kilogram for bismuth trioxid. When this amount of the respective drugs was injected intramuscularly, the results obtained conformed in a general way to the foregoing standard, except that twenty-four hours after the injection more motile spirochetes were seen in the dark-field than are present twenty-four hours after an intravenous injection of 0.006 gm. of arsphenamin. However, dark-field examination conducted on subsequent days were negative, and the syphilitic lesion involuted within the specified time. This can doubtless be explained by the different methods employed in administering the bismuth preparations.

The maximum tolerated and lethal doses of the bismuth preparations were determined by injecting intramuscularly into normal rabbits increasing amounts of the respective drugs. The maximum tolerated dose [26] of sodium and potassium tartrobismuthate in aqueous solution was 0.125 gm. per kilogram. The majority of animals injected with 0.150 gm. and larger amounts per kilogram died. With the oil suspension of the drug, animals survived doses up to 0.2 gm. per kilogram, but succumbed to injections of 0.25 gm. Animals injected with potassium tartrobismuthate survived doses up to 0.25 gm. per kilogram,[27] but died following injections of 0.3 gm. The maximum tolerated dose of bismuth trioxid in olive oil was 0.4 gm. per kilogram. Animals injected with 0.45 gm. and larger amounts per kilogram died.

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25. In some animals, active syphilitic lesions recur after this period.

26. The majority of rabbits after receiving the maximum tolerated dose of the bismuth preparations lost from 300 to 400 gm. in weight during about two weeks following the injection. After this time the weight gradually increased up to about the weight before treatment.

27. There was one exception to this: one animal died after an injection of 0.15 gm. per kilogram; however, all other animals injected survived this dose, and none of the animals injected with doses of 0.2 and 0.25 gm. died.

The maximum tolerated dose of potassium tartrobismuthate was about five times the therapeutic active dose; with an oil suspension of sodium and potassium tartrobismuthate, it was four times the therapeutic active dose; with an aqueous solution of the same drug, it was two and one-half times the therapeutic dose; and with bismuth trioxid in olive oil, it was a little more than two and one-half times the therapeutic active dose.

Since the recorded therapeutic active and maximum tolerated doses of mercury and of arsphenamin are based on the intravenous administration of these drugs, their spirocheticidal action cannot be compared accurately with that of bismuth. According to Nichols,[28] the maximum tolerated dose of mercuric chlorid when injected intravenously into rabbits is 0.001 gm. per kilogram; the therapeutic active dose in syphilitic rabbits is 0.003 gm. per kilogram. The therapeutic active dose of arsphenamin injected intravenously into syphilitic rabbits is about 0.006 per kilogram; the maximum tolerated dose is about 0.1 per kilogram.

The aforementioned therapeutic active and maximum tolerated doses of sodium and potassium tartrobismuthate in aqueous solution and in oil suspension are about the same as reported by Sazerac and Levaditi.[4] The therapeutic active and maximum tolerated doses of the other two bismuth preparations studied have not to my knowledge been studied and reported by others.

THE HERXHEIMER REACTION AFTER BISMUTH ADMINISTRATION IN EXPERIMENTAL SYPHILIS

Occasionally after the intravenous injection of the therapeutic active dose of the arsphenamins in syphilitic rabbits with active testicular lesions, the testicles become considerably enlarged and the scrotum edematous. The organ becomes two or three times its size before treatment. This reaction occurs within twenty-four hours after the first treatment and subsides in a few days. This phenomenon doubtless represents what may be regarded as a local Herxheimer reaction, as it is in all probability a reaction due to the lysis of spirochetes by a powerful spirocheticidal drug.[29]

Such a reaction was observed in this study appearing forty-eight hours after an intramuscular injection of 0.05 gm. per kilogram (therapeutic active dose) of potassium tartrobismuthate. The testis enlarged to about three times its size before treatment (Fig. 6), although the reaction appears within twenty-four hours after an intravenous injec-

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28. Nichols, H. J.: Further Observations on Certain Features of Experimental Syphilis and Yaws in the Rabbit, J. Exper. Med. **14**:202, 1917.

29. In a personal communication, Dr. Wade Brown concurs with me in this opinion.

tion of arsphenamin, its occurrence forty-eight hours after an intramuscular injection of potassium tartrobismuthate can be explained by the different method of administering this drug.

The occurrence of this reaction after bismuth treatment doubtless furnishes additional evidence that bismuth exerts a powerful spirocheticidal action.

SPIROCHETICIDAL ACTION OF BISMUTH INUNCTIONS IN RABBIT SYPHILIS

It was observed by Levaditi that the oral administration of sodium and potassium tartrobismuthate in syphilitic rabbits did not exert a notable spirocheticidal action. By rectal administration, its spirochet-

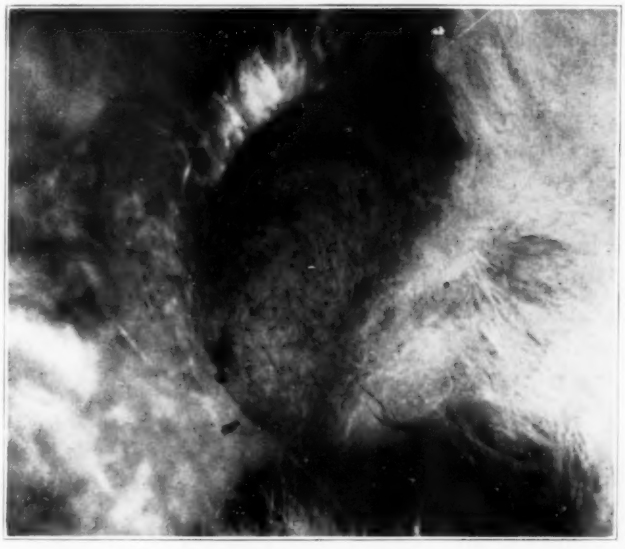

Fig. 6.—Considerably enlarged testis and edematous scrotum of syphilitic rabbit, which occurred forty-eight hours after an intramuscular injection of 0.05 gm. per kilogram of body weight of potassium tartrobismuthate.

icidal action was greater. He also observed that 33 per cent. of this drug in ointment form exerted an active spirocheticidal action when applied locally.

In this study, experiments were conducted on rabbits with active syphilitic testicular lesions to determine whether bismuth administered in the form of inunctions exerted a spirocheticidal action. Bismuth trioxid was employed in 2 gm. each of benzoated lard and petrolatum. Varying amounts of the drug per kilogram were used. One side of the animals treated was shaved and the ointment rubbed in for twenty

minutes. It was observed that 0.5 gm. of bismuth trioxid per kilogram administered daily in inunctions for five consecutive days [30] exerted a spirocheticidal action which conformed to the standard adopted in studying the bismuth preparations, except that the dark-field examination the day following the initial inunction disclosed many motile spirochetes in each microscopic field; the examination on the third and fourth days showed a few nonmotile organisms.[31] The syphilitic lesion, however, was completely involuted by the eighth day.

COMPARATIVE VALUE OF THE BISMUTH PREPARATIONS STUDIED; COMPARISON WITH ARSPHENAMIN AND WITH MERCURY

The comparative value of the bismuth preparations employed in this study, so far as the therapeutic active and maximum tolerated doses in syphilitic and in normal rabbits are concerned, has already been discussed. The comparative value so far as the percentage of bismuth is concerned, has likewise been given. It should be noted that although the ratio between the therapeutic active and maximum tolerated dose of potassium tartrobismuthate was greater than that of sodium and potassium tartrobismuthate and bismuth trioxid, and that it contained more bismuth than sodium and potassium tartrobismuthate, yet it was not more therapeutically active in the treatment of rabbit syphilis.

It has not yet been possible, owing to the relatively short period of our observations, to determine the comparative value of the bismuth preparations in the treatment of syphilis. As noted in the foregoing and further shown in Cases 2, 3 and 4, the three preparations employed appeared to exert equal spirocheticidal action.

The use of an oil suspension of sodium and potassium tartrobismuthate is to be preferred to an aqueous solution by virtue of it being less painful. This advantage also applies to bismuth trioxid, which was injected in olive oil.

One injection of bismuth trioxid produced less immediate effect on an active syphilitic lesion than one injection of the same amount of the other two bismuth preparations. This can doubtless be explained by the delayed absorption of this drug, since it is insoluble, whereas the other preparations are soluble. For the same reason, suddenly appearing stomatitis and other untoward reactions following the use of bismuth trioxid, although not observed in this study, is a theoretical possibility. The end result of treatment with bismuth trioxid appeared to be the same as with the two other preparations, that is, about the

30. After receiving this treatment the animal lost 300 gm. in weight.

31. Larger amounts up to 1 gm. per kilogram of bismuth trioxid did not influence the rate of disappearance of spirochetes in the dark-field examination.

same total amount of bismuth trioxid was required to effect the disappearance of syphilitic lesions and to cause positive Wassermann reactions to become negative, as was required with the two other preparations.

The results of the studies herein reported have left no doubt as to the spirocheticidal action of the bismuth preparations employed. This action is greater than that of mercury but less than that of arsphenamin, although a clinical comparison of the spirocheticidal action of arsphenamin with that of bismuth cannot accurately be made, since arsphenamin is administered intravenously in a much larger amount than is bismuth which is administered intramuscularly.

As to its spirocheticidal action, bismuth can be placed about midway between mercury and arsphenamin. In this regard, Milian compares the therapeutic activity of arsphenamin, bismuth and mercury in this way: The therapeutic activity of arsphenamin is represented by the figure 10, bismuth by the figure 7 and mercury by the figure 4.

ADVANTAGES OF BISMUTH THERAPY AS COMPARED WITH ARSPHENAMIN THERAPY

Space will not permit a detailed discussion as to the advantages of bismuth therapy in human syphilis as compared with arsphenamin therapy.

The advantage of having another active antisyphilitic drug in the treatment of human syphilis is obvious. Bismuth therapy is particularly advantageous in the treatment of syphilitic patients who are hypersensitive to arsphenamin so that the use of the latter drug is restricted or contraindicated, or when for other reasons arsphenamin cannot be administered.

Another possible advantage of bismuth in the treatment of syphilis which is of considerable importance, although based on theoretical considerations, concerns the occurrence of neurorecidive following the use of arsphenamin. The baneful action of irregular or lapsing treatment with arsphenamin is well known. Such treatment greatly increases the incidence of early neurosyphilis. Ehrlich's explanation of this phenomenon is perhaps the one generally accepted. He explained the occurrence of neurorecidive on an immunologic basis. He pointed out that "In these patients the greater number of spirochetes are destroyed by the powerful spirocheticidal action of arsphenamin. So rapidly is this accomplished that the usual tissue immunity which develops as a result of contact between parasite and host is lacking; as a result a small focus of spirochetes in the tissue of the central nervous system which may escape the action of salvarsan develops in the susceptible

host with great rapidity and severity."[32] In other words, a few injections of arsphenamin and the cessation of all other treatment inhibit the consummation of immunologic responses of the host to the parasite, and doubtless produce a condition analogous to that existing in the primary incubation period, in which there are spirochetes and no immunologic reaction.[33]

Bismuth, on the other hand, by reason of less energetic spirocheticidal action than arsphenamin and perhaps by virtue of intramuscular administration, does not, in all probability inhibit immunologic reaction of the host to such an extent as it is believed that arsphenamin does. One would, therefore, expect a lessened incidence of early neurosyphilis following irregular and lapsing treatment with bismuth.

SUMMARY

This report is based on an experimental study of bismuth as a spirocheticidal drug in rabbit syphilis. The relation between the therapeutic active dose and the lethal dose is discussed; and the clinical results from the use of bismuth in the treatment of fifty syphilitic patients in the three stages of syphilis, the majority of whom presented a cutaneous manifestation of the disease. The bismuth preparations employed were the French preparation of sodium and potassium tartrobismuthate in aqueous solution and in olive oil, potassium tartrobismuthate in aqueous solution and bismuth trioxid in olive oil and by inunctions.

The chemistry of the bismuth tartrates is discussed.

All of the bismuth preparations employed in the study were administered intramuscularly. Intravenous administration is positively contraindicated. The doses of the bismuth preparations employed ranged from 0.1 gm. to 0.2 gm., the interval between injections ranged from every other day to every fourth day. The total amount of the bismuth

32. An analogous phenomenon has been produced in experimental syphilis as shown in the work of Brown and Pearce (The Resistance [or Immunity] Developed by the Reaction to Syphilitic Infection, Arch. Dermat. & Syph. **2**: 675 [Dec.] 1920). The spontaneous occurrence of generalized syphilis in rabbits following testicular inoculation is exceptional. Brown and Pearce have shown that the primary testicular reaction plays an important defensive rôle in preventing generalized syphilis in the rabbit. They succeeded in generalizing syphilis by suppressing this local primary tissue reaction. The administration of subcurative doses of spirocheticidal drugs was one method of suppressing this local reaction.

33. It is interesting to recall that the older syphilologists awaited the appearance of secondary manifestations of syphilis, not only for diagnostic purposes, but in order not to interfere with the orderly progression of the disease as it concerned the consummation of immunologic responses.

preparations employed that can be well tolerated in a specified time cannot be stated arbitrarily. In this study, this amount ranged from 1 gm. in exceptional cases, to about 2.5 gm. The majority of patients will perhaps tolerate about 2 gm. in one month without developing any untoward reactions.

Untoward reactions of bismuth therapy in syphilis are given. A foul breath and a gingival blue line, which forecast the appearance of stomatitis, are particularly stressed.

Lesions of primary, secondary and tertiary syphilis were involuted after a total administration of the bismuth preparations employed, in amounts ranging from 0.3 gm. to 1.5 gm.

The four plus Wassermann reaction of patients in early secondary and late secondary stages of syphilis became negative, in the majority of cases, following a total administration of about 2 gm. of the bismuth preparations employed. Other patients, however, required 3 gm. or more before the Wassermann test became negative. The four plus reaction of primary syphilis became negative after a lesser amount of the drug, and was somewhat proportional to the duration of the chancre. The four plus Wassermann reaction of tertiary syphilis required varying amounts of bismuth treatment and cannot be stated arbitrarily. In two patients in the early stage of syphilis, there was an early recurrence of a positive Wassermann reaction after the cessation of treatment.

The antisyphilitic effect of bismuth is noted for some time after the administration of the drug.

The pain and local reaction following an injection of the bismuth preparations was variable. An aqueous solution of sodium and potassium tartrobismuthate was more painful than an oil suspension. Potassium tartrobismuthate was injected with a local anesthetic—butyn—the pain after injection was negligable. Injections of bismuth trioxid in olive oil were not painful.

Knowledge of the distribution of bismuth and its elimination when injected intramuscularly is reviewed.

The employment of 50 per cent. bismuth inunctions in the treatment of human syphilis exerted a feeble spirocheticidal action.

The observations of Sazerac and Levaditi on the spirocheticidal action of bismuth in experimental syphilis was confirmed. The therapeutic active and maximum tolerated doses of the bismuth preparations studied in syphilitic and normal rabbits are given. Bismuth applied in the form of inunctions to syphilitic rabbits exerted a spirocheticidal action.

It was not possible in the brief duration of the clinical study to determine the comparative value of the bismuth preparations employed. The three preparations appeared to exert equal spirocheticidal action in

the treatment of human syphilis. So far as its spirocheticidal action is concerned, bismuth can be placed about midway between mercury and arsphenamin.

Bismuth therapy is particularly advantageous in the treatment of syphilitic patients who are hypersensitive to arsphenamin so that the use of the latter drug is restricted or contraindicated. Neurorecurrence, appearing after irregular and lapsing treatment with the arsphenamins is briefly discussed. Bismuth, by virtue of its exerting a less energetic spirocheticidal action than arsphenamin, does not in all probability inhibit the immunologic reaction of the host to such an extent as it is believed arsphenamin does. One would, therefore, expect a lessened incidence of early neurosyphilis (neurorecidive) following irregular and lapsing treatment with bismuth.

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BISMUTH IN THE TREATMENT OF SYPHILIS*

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NEW YORK

In January, 1922, Levaditi and Sazerac [1] reported a series of observations on the treatment of syphilis by the various bismuth salts. The possible usefulness of bismuth had been suggested to them by an earlier paper of Sauton and Robert [2] on the prophylaxis and treatment of spirochetosis of fowls by bismuth salts.

Levaditi and Sazerac's experiments included a series of tests on rabbits for toxicity and spirocheticidal action, and a few observations on the treatment of human syphilis. In their preliminary work, they examined the action of a number of bismuth salts, including the citrate, lactate, subgallate and a quadruple salt referred to as potassium sodium tartarobismuthate. In regard to toxicity, they found in general that the soluble salts were more toxic than the insoluble and far more toxic when injected intravenously than when injected subcutaneously. Of all, the tartarobismuthate was the least toxic. If suspended in oil and injected into the muscles, 400 mg. per kilogram of body weight was found to be well tolerated. The same salt given by the same route in an alkaline aqueous solution was well borne in doses of 50 mg. per kilogram, but invariably fatal in doses of 200 mg., whereas when injected intravenously, 10 mg. killed the animal in three days.

For determining spirocheticidal power, they used rabbits infected with human syphilis and also with *Spirochaeta cuniculi*. They found that doses of 100 mg. of tartrobismuthate per kilogram caused a disappearance of the spirochetes in twenty-four hours and healing of the lesions on the second or fourth day. In one animal observed for four months, there was no relapse.

In early active human syphilis they found that intramuscular injections caused prompt involution of the lesions, disappearance of the spirochetes and reversion of the Wassermann reaction from positive to negative. In rabbits, cures were also obtained by intravenous injection and improvement by local inunction. Administration by mouth or by rectum was ineffective. On account of the toxicity of the soluble compounds, especially when given intravenously, they recommend for trial in human cases intramuscular injections of quadruple salt.

Simultaneously with this paper of Levaditi and Sazerac there appeared a clinical report by Fournier and Guénot [3] on the use of the latter preparation in about 200 cases of syphilis. They reported that chancres were as rapidly improved by bismuth as by any other form of treatment and disappeared entirely

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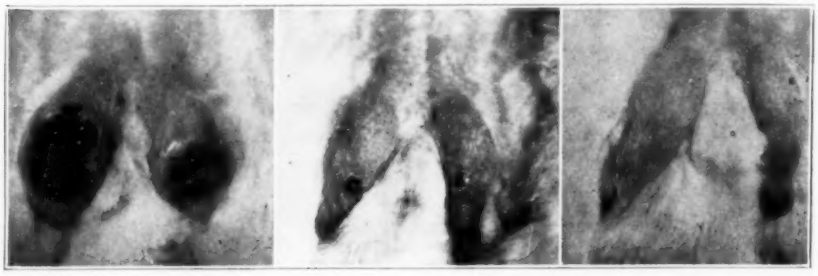
1. Levaditi and Sazerac: Ann. Pasteur Inst. **36**:1, 1922.
2. Sauton and Robert: Ann. Pasteur Inst. **30**:261, 1916.
3. Fournier and Guénot: Ann. Pasteur Inst. **36**:14, 1922.

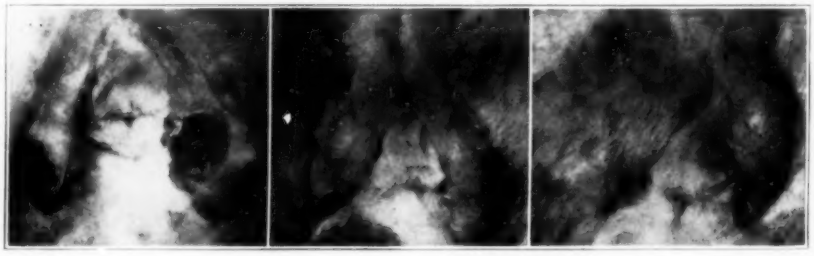
in a few weeks. They also found a prompt conversion of a positive Wassermann reaction to a negative, the reaction remaining negative during the period of observation. In cases of secondary syphilis, the skin and mucous membrane lesions healed about as rapidly as with arsenicals. In some instances, they noted a temporary exacerbation of the symptoms (Herxheimer reaction). In the secondary cases also the Wassermann reaction cleared up satisfactorily. In cases of late syphilis, the cutaneous and periosteal lesions healed with the same rapidity, although in some instances the serum reaction was unaffected.

They observed no serious toxic effects. The majority of the patients showed a bluish line along the border of the gum similar to that seen in lead poisoning,



A B C

Fig. 1. (Rabbit Bi7).—Treated with tartrobismuthate, 100 mg. per kilogram. *A*, extensive induration and large ulcers before treatment; *B*, induration gone and ulcers nearly healed eighteen days after treatment; *C*, normal appearance six weeks after treatment.



A B C

Fig. 2 (Rabbit Bi9).—Treated with tartrobismuthate, 25 mg. per kilogram. *A*, moderate induration and large ulcers before treatment; *B*, induration gone and ulcers nearly healed two weeks after treatment; *C*, normal appearance four weeks later.

and in a number of cases gingivitis or stomatitis developed, in the production of which the bacillus and spirillum of Vincent seemed to be involved. They reported that the stomatitis was improved by local administration of the quadruple bismuth salt, and was probably produced by the secretion of bismuth in the saliva as a sulphid which was not spirocheticidal. In a few cases, they noted a temporary polyuria and albuminuria, but never any persistent evidence of disturbed renal function. The chief inconvenience was the pain

at the site of injection, which was similar to that caused by insoluble preparations of mercury. They were able to find bismuth in the blood, cerebrospinal fluid, the saliva, the bile, feces, sweat and urine of patients under treatment.

Another brief clinical report by Marie and Fourcarde[4] on the treatment of syphilis of the nervous system with bismuth appeared in the same number of the *Annales*. They say frankly that their patients were observed for too short a time to admit of definite conclusions in this type of case. Most of them were suffering from advanced general paresis. In these no symptomatic or serologic change was noted. On the other hand, in a few patients with vascular or nerve root lesions or with gumma of the central nervous system, there was prompt and definite improvement.

More recently the action of other bismuth preparations has been studied, none of which appears to be much more effective than the salt originally employed, but which are claimed to cause less pain and consequently to permit of somewhat larger dosage. Levaditi and Sazerac[5] reported in April that suspensions of bismuth element also had a satisfactory curative effect on rabbits. Fournier and Guénot[6] soon after reported on the effect of this prepara-

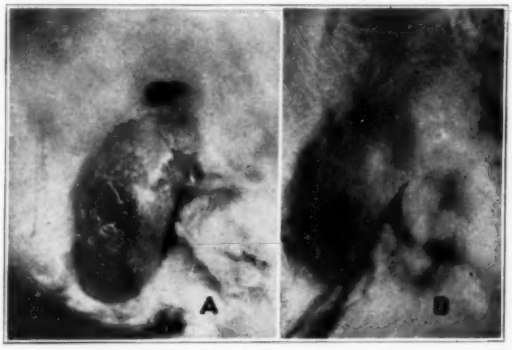


Fig. 3 (Rabbit As4).—Treated with neo-arsphenamin, 15 mg. per kilogram. *A*, extensive induration with two ulcers before treatment; *B*, induration gone and ulcers healed eighteen days after treatment.

tion on human cases, and their findings that primary or secondary lesions disappeared after two or three injections, that the drug was well borne and that it had a striking effect in clearing up the Wassermann reaction.

Since the appearance of these reports, the French journals have carried many brief communications in regard to the treatment of syphilis by various bismuth preparations. At the first congress of French speaking dermatologists and syphilographers held in Paris in June, 1922,[7] there were thirteen separate reports on this subject from various clinics in France, Spain, Brazil, and Denmark, all of which reported striking therapeutic results from the use of this drug.

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4. Marie and Fourcarde: Ann. Pasteur Inst. **36**:34, 1922.
5. Levaditi and Sazerac: Compt. rend. Soc. de biol. **86**:817, 1922.
6. Fournier and Guénot: Compt. rend. Soc. de biol. **86**:908, 1922.
7. Presse méd. **30**:582, 1922.

One report has come from Germany by Müller,[8] who states that the curative effect of the tartrobismuthate is as rapid as that of arsphenamin. Sedlak[9] of Prague has reported favorable results in a series of seventy-six cases treated with arsphenamin and bismuth combined.

The only report that has as yet been found in American journals is one by Villemin of Nice,[10] in which he gives a brief review of the subject and a report of his own experiences, with quinin bismuth iodid.

The work of these various observers seems to have established that bismuth possesses curative powers in syphilis. Its practical value in the treatment of the disease in man will have to be determined by long and careful observation. So far, there appears to have been little interest in the subject in this country and a report of a brief experience in its use may be of value. Some statement of facts concerning it seems to be especially necessary since manufacturers are already dis-

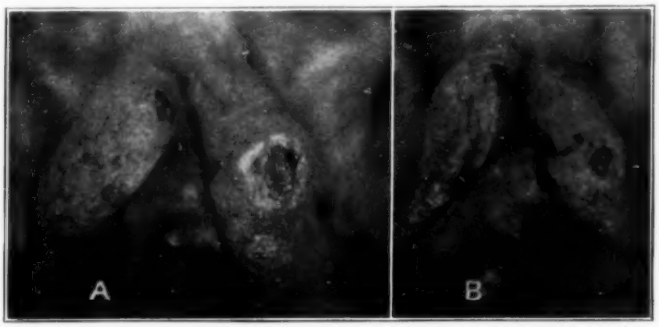

Fig. 4 (Rabbit Bi6).—Treated with tartrobismuthate, 100 mg. per kilogram. *A*, extensive induration and moderate sized ulcers before treatment; *B*, induration gone and ulcers nearly healed two weeks after treatment.

tributing circulars in which they describe with typical commercial optimism the curative powers of their particular preparations of bismuth.

The forms of bismuth which have been given clinical trial are:

(1) The sodium and potassium tartrobismuthate which is sold under various trade names. The method of preparation is given on page 749. It contains about 50 per cent. of bismuth. The dosage for active cases recommended by Fourner and Guénot is from 0.2 to 0.3 gm. injected intramuscularly two to three times a week, reaching a total of 2 to 3 gm. during the first month. After this first series treatment is continued by the injection of 0.2 to 0.3 gm. once a week. In sensitive patients, the dose may be reduced to 0.1 gm.

(2) Bismuth element in fine suspension, which has also been given trade names, prepared by reduction of the quadruple salt. The detailed method of

8. Müller: München. med. Wchnschr. **49**:547, 1922.
9. Sedlak: Quoted in Bull. de Inst. Pasteur **20**:851, 1922.
10. Villemin: Urol. & Cutan. Rev. **27**:11, 1923.

preparation has not been published. It is recommended by Fournier and Guénot in doses of 0.15 to 0.2 gm. injected intramuscularly twice a week for a series of ten to twelve injections. This introduces nearly twice as much bismuth as their dosage for the quadruple salt.

(3) Quinin bismuth iodid. We have not been able to find a statement of its chemical composition or method of preparation, but the substance is probably similar to that thrown down in Léger's test for bismuth. It is said to contain 30 per cent. of the element. The course of treatment recommended by Villemin consists of intramuscular injections of from 0.2 to 0.3 gm. every two days for twelve injections.

(4) Colloidal bismuth. The method of preparation is not described. It is advocated by Galliot,[11] who employs intravenous injections of 8 c.c. increasing the dosage to 24 c.c. three times a week, followed by weekly injections of from 16 to 20 c.c. Galliot was impressed by the therapeutic action of this preparation, although the actual amounts of bismuth introduced are small, 0.013 gm. being the maximum dosage.

Grenet and Drouin[12] have reported results of experiments with a compound of phenol and bismuth.

Bismuth hydroxid[13] and other preparations have also been used, but no conclusive observations have been reported. In fact, the only preparations as to the value of which detailed evidence is yet available are the first two mentioned.

PREPARATION

The observations which we wish to report concern only the quadruple salt first recommended by Levaditi. It was prepared by the following method described by Cowley:[14]

Bismuth subnitrate	70	gm.
Sodium and potassium tartrate	64.5	gm.
Nitric acid (specific gravity, 1.430)	57	c.c.
Sodium bicarbonate	57	gm.

Mix the nitric acid with an equal volume of water and dissolve the bismuth subnitrate. Add the Rochelle salts dissolved in a little water and then the sodium bicarbonate also dissolved in water. Heat to expel carbon dioxid, filter and wash the precipitate until the filtrate no longer gives a test for nitrates. The product is an amorphous white substance which turns brown on overheating or exposure to light. It has a peculiar mortar-like consistence which makes it difficult to grind to a fine smooth powder or to obtain a smooth suspension in oils. Dr. J. H. Mueller kindly assayed one of our preparations and found it contained 54.2 per cent. of bismuth.

For the treatment of patients we have tried 10 and 20 per cent. suspensions. The formula which we are using at present is

Sodium and potassium tartrobismuthate	10 gm.
Anesthesin	10 gm.
Coconut oil	80 gm.

Dosage: One to two c.c. equal to 1 or 2 decigrams.

11. Galliot: Jour. de méd. de Paris **41**:513, 1922.
12. Grenet and Drouin: Compt. rend. Acad. d. sc. **174**:647, 1922.
13. Fourcade, Jaloustre and Lemay: Compt. rend. Soc. de biol. **86**:815, 1922.
14. Cowley: Chemist and Druggist **82**:212, 1913.

EXPERIMENTS IN ANIMALS

In order to form an opinion as to the efficacy of this substance it seemed advisable to compare its action in syphilitic rabbits with that of drugs which are known to be effective in human syphilis. We selected as representative substances for this comparison neo-arsphenamin and mercuric salicylate. The rabbits were infected with a strain of *Spirochaeta pallida* isolated from human spinal fluid by Nichols in 1912. On this occasion, we obtained it through the courtesy of Dr. Wade H. Brown.

For some of our observations we employed rabbits inoculated into the scrotal tissue in such a way as to produce large ulcers, changes in which were easy to observe and to record photographically. As such lesions are hyperemic and often secondarily infected, it is occasionally difficult to demonstrate the spirochetes even when the disease is progressing. Consequently, other tests were made on animals inoculated

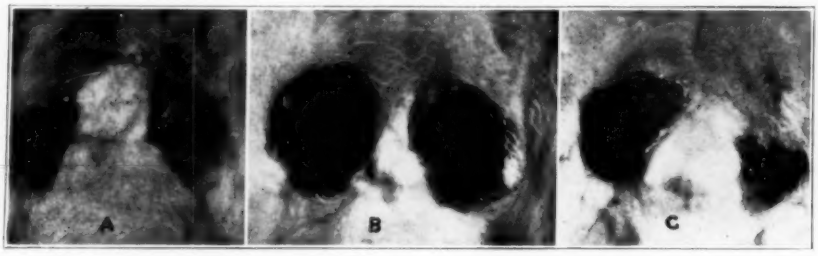

Fig. 5 (Rabbit C2).—Untreated control for Bi4, Bi6, Bi9 and Hg3. *A*, large scrotal ulcers six weeks after inoculation; *B*, four weeks later, ulceration extending; *C*, eight weeks later, scrotum nearly destroyed.

into the testicle so as to produce deep nodular lesions with a poor blood supply in which the spirochetes can be demonstrated more regularly when present. Frequently these animals also developed ulcers at the site of puncture by the inoculating needle or by extension from a testicular lesion.

In treatment, the neo-arsphenamin was dissolved in distilled water and injected into the ear vein; the bismuth and mercury salts were suspended in olive oil and injected into the erector spinae muscles.

CONTROLS

We had previously studied this same strain of spirochetes in passage through rabbits for three years and were familiar with the course of untreated lesions. Indurated testicular lesions of the type used frequently heal spontaneously, but involution is slow and hardly to be confused with the abrupt softening observed in successfully treated

animals. The cutaneous ulcers are more persistent and frequently progress until the entire scrotal tissue is destroyed. In these experiments, each lot of animals inoculated were treated one or two at a time, and the untreated members of the group served for a while as controls for those treated. On account of the persistence of the lesions, however, it seemed safe later to use these controls as test animals. Only a few were held untreated throughout the experiment. The course in two of these is shown in Figures 5 and 6. The only spontaneous cure observed occurred three months after the other rabbits of the same set had been tested.

EFFECT IN MAXIMUM DOSAGE

Our first effort was to compare the action of the three drugs used in maximum dosage.

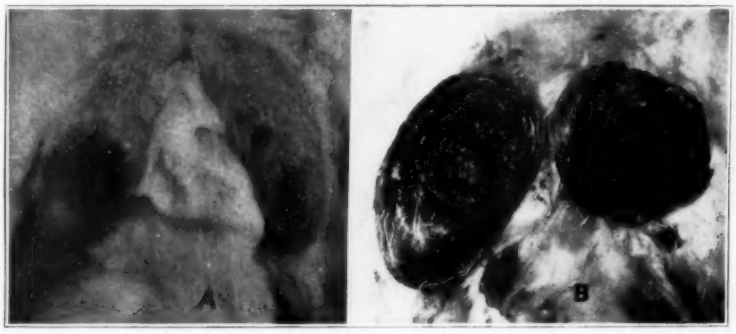

Fig. 6 (Rabbit C1).—Untreated control for Bi7, As2, As4 and Hg2. *A*, six weeks after inoculation; *B*, eight weeks later, ulceration extending.

For the sodium and potassium tartrobismuthate we started from the statement of Levaditi and Sazerac that 400 mg. per kilogram was nontoxic for a rabbit. In our preliminary tests, a normal rabbit which was given 200 mg. per kilogram died in six days, and one which received 100 mg. survived, so that we selected the latter amount as our maximum dose. Further experience showed that this was probably more than could safely be given.

For neo-arsphenamin Castelli[15] gives 300 mg. per kilogram as the tolerated dose, and we used one half this amount—150 mg.

For mercuric salicylate no experimental data were available, and we selected an amount which gave no immediate toxic symptoms—30 mg. per kilogram.

The effects of such injections are shown in Table 1.

15. Castelli: Ztschr. f. Immunitätsforschung **1**:321, 1913.

TABLE 1.—*Comparative Effect on Experimental Lesions in Rabbits of Treatment by Single Injections of Sodium and Potassium Tartrobismuthate, Neo-Arsphenamin and Mercuric Salicylate*

BISMUTH SERIES

No.	Period Since Inoculation	Condition Before Treatment	Dose per Kilogram	Condition After Treatment	Last Observation
Bi 1	4 months	1.5 cm. ulcer left scrotum; spirochetes numerous	100 mg.	1st and 2d day, spirochetes 0; 5th day, induration diminished; ulcer healed in 4 weeks	8th week, normal
Bi 2	4 months	1 cm. nodule in left testis; two ulcers, 1 cm. in right scrotum; spirochetes present	100 mg.	2d day, spirochetes 0; 5th day, ulcers beginning to heal	5th day, dead; lesions improved
Bi 3	2 months	1 cm. nodules on right and left scrota; spirochetes numerous	100 mg.	1st and 2d day, spirochetes 0; 5th day, induration diminished; 4th week, testicles normal	4th week, normal
Bi 4	5 weeks	Large ulcers on both scrota with underlying nodules in testes; spirochetes numerous	100 mg.	1st, 2d and 3d day, spirochetes 0; 3d day, induration diminished	2d week, dead; ulcers nearly healed
Bi 5	4 weeks	Moderate sized ulcers on both scrota; spirochetes numerous	100 mg.	1st day, few spirochetes; 2d day, none; 6th day, induration gone, ulcers improved; animal killed on account of injury	6th day, improved
Bi 6	7 weeks	Diffuse induration in both testes with scrotal ulcers; spirochetes present	100 mg.	2d day, spirochetes 0; 4th day, induration diminished	3d week, dead; ulcers nearly healed
Bi 7	6 weeks	Large ulcers on both scrota; spirochetes present	100 mg.	1st week, ulcers improved, induration nearly gone; 7th week, entirely healed	13th week, normal
Bi 8	4 weeks	Small nodule in right testis; hydrocele of left scrotum; spirochetes present	100 mg.	2d day, spirochetes 0; nodule diminished; 1st week, gained 300 gm.; 4th week, normal	12th week, normal
Bi 9	7 weeks	1.2 cm. ulcers on both scrota	25 mg.	4th day, ulcers healing; 3d week, normal	4th week, normal
Bi 10	5 weeks	Two nodules in left testis; large mass in right testis with ulceration of scrotum; spirochetes present	5 mg.	3d day, spirochetes 0; induration diminished; 12th day, induration gone; 3d week, ulcer healed	11th week, normal
Bi 11	5 weeks	Large mass left testis with 1.2 cm. scrotal ulcer; nodule right testis with small scrotal ulcer; spirochetes present	2 mg.	3d day, spirochetes present; induration diminished; 6th day, spirochetes 0; 10th day, ulcers healed; 5th week, induration gone, small ulcer in scar, spirochetes 0, probably due to secondary infection	5th week, normal (?)
Bi 12	5 weeks	Diffuse induration of both testes; spirochetes numerous	2 mg.	1st day, spirochetes present; 3d day, spirochetes 0, induration diminished; 19th day, induration gone	19th day, normal
Bi 13	6 weeks	Hard nodules both testes with infiltration of scrota and beginning necrosis on right; spirochetes present	2 mg.	5th day, spirochetes 0; 4th week, nodules gone	6th week, normal
Bi 14	4 weeks	Induration and positive puncture three weeks after inoculation; at time of treatment edema of testes; spirochetes 0	2 mg.	1st and 5th day and 5th week, spirochetes 0; 7th week, developed nodules containing spirochetes	7th week, positive lesion
Bi 15	6 weeks	Diffuse infiltration of right testis and scrotum; large ulcer on left scrotum; spirochetes numerous	1 mg.	4th day, 6th day and 2d week, spirochetes present; lesions steadily progressing	2d week, ulceration extending

TABLE 1.—*Comparative Effect on Experimental Lesions in Rabbits of Treatment by Single Injection of Sodium and Potassium Tartrobismuthate Neo-Arsphenamin and Mercuric Salicylate—Continued*

NEO-ARSPHENAMIN SERIES

No.	Period Since Inoculation	Condition Before Treatment	Dose per Kilogram	Condition After Treatment	Last Observation
As 1	2 months	Nodules in both testes; spirochetes present	150 mg.	1st day, spirochetes 0; 6th day, induration diminished	9th day, dead; lesion improved
As 2	6 weeks	1.5 cm. ulcers on both scrota	150 mg.	7th day, ulcers healing; 10th day, induration gone; 18th day, completely healed	18th day, dead; lesions healed
As 3	4 weeks	Diffuse induration of left testis and nodule in right; spirochetes numerous	150 mg.	1st and 3d day, spirochetes 0; 7th day, induration gone	7th day, dead; lesions healed
As 4	6 weeks	Large mass in right testis with two small scrotal ulcers	15 mg.	7th day, induration diminished; 10th day, induration gone; 18th day, ulcer healed	13th week, normal
As 5	5 weeks	Diffuse induration of right testis with 1.5 cm. scrotal ulcer; spirochetes present	6 mg.	1st day, spirochetes present; 3d, 7th and 12th day, spirochetes 0; 3d day, induration diminished; 14th day, induration gone; 4th week, ulcer healed	4th week, normal
As 6	5 weeks	Several nodules in right testis; 0.5 cm. ulcer on left scrotum; spirochetes numerous	3 mg.	3d day, spirochetes present; 7th day, spirochetes 0; 12th day and 2d week, spirochetes present; slight improvement during first week after which lesions steadly progressed	4th week, ulceration and induration extending
As 7	8 weeks	Large nodules in left testis; spirochetes present	1.5 mg.	3d day and 1st week, spirochetes present; lesions progressed without interruption	3d week, induration and ulceration extending

MERCURIC SALICYLATE SERIES

Hg 1	2 months	Induration of both scrota; spirochetes present	30 mg.	1st and 2d day, spirochetes 0; 4th day, dead; induration slightly diminished	4th day, dead; lesions slightly improved
Hg 2	6 weeks	1 cm. ulcer on left scrotum; 0.5 cm. ulcer on right scrotum with marked induration	30 mg.	6th day, animal dead, induration diminished and ulcer nearly healed	6th day, dead; lesions improved
Hg 3	5 weeks	Large ulcers on both scrota; spirochetes present	30 mg.	1st and 2d day, spirochetes 0; 6th day, animal very ill, ulcers healing	13th day, dead; ulcers nearly healed
Hg 4	7 weeks	Induration of right scrotum with small ulcer; spirochetes present	15 mg.	5th day, animal dead of enteritis and tubular nephritis; induration gone, ulcer healed	5th day, dead; lesion healed
Hg 5	7 weeks	Induration of left testis with small scrotal ulcer; spirochetes present	6 mg.	5th day, spirochetes 0; induration diminished, ulcer healed; 4th week, relapse, induration marked, spirochetes present; 8th week, induration gone, spirochetes 0, animal much emaciated, killed, no evidence of enteritis or nephritis	8th week, normal after relapse
Hg 6	5 weeks	Diffuse induration of both testes, with beginning necrosis of scrota; spirochetes present	3 mg.	5th day, spirochetes 0; 9th day, induration slightly diminished but ulcer developed in scrotum, this extended until in 9th week scrota were completely destroyed; from 11th day on spirochetes present	9th week, lesions extending
Hg 7	5 weeks	Large ulcers on both scrota; spirochetes present	1.5 mg.	Ulceration extended without interruption to complete destruction of scrota in 9 weeks	9th week, lesions extending

After a large injection of bismuth, the organisms disappeared promptly from the lesions and were not found later than the first day after treatment. Deep nodules were perceptibly softened on the second to fifth day and not palpable after a week or ten days. In large scrotal ulcers, repair was much slower. A lessening of the underlying induration was apparent in from four to five days, after which a conical slough was gradually separated. The ulcer then contracted, and in two weeks all that remained was a small superficial defect covered by a thin crust. This, in some cases, persisted for several weeks before healing was complete. Healing required more time than in the rabbits tested by Levaditi and Sazerac, a discrepancy which might well be accounted for by differences in the character of the lesions.

The immediate effects of neo-arsphenamin and mercury were indistinguishable from those of bismuth. Such differences in reaction as were noted during the first week seemed to depend more on the character of the lesion than on the drug used.

Rabbits Bi 7 and As 2 had lesions which matched well. One was treated with bismuth and the other with neo-arsphenamin; their condition at first progressed closely in parallel. The rabbit treated with arsphenamin died on the eighteenth day with the lesions completely healed, at which time only a minute linear ulceration remained on one side in the animal treated with bismuth.

It soon became evident that the doses used were too large. The animals treated with mercury died in from four to thirteen days; those given neo-arsphenamin, in from seven to eighteen days. Of the rabbits treated with bismuth, one died in five days, one in two weeks, and one in three weeks; but four survived as long as they were kept under observation.

THE CURATIVE DOSE

These experiments sufficed to show that bismuth as well as the other drugs was spirocheticidal and had a curative effect. In order to form some idea of their relative value, it was attempted to determine the smallest curative dose of each of the three substances. For our purpose, we defined this dose as the amount necessary to cause spirochetes to disappear and active lesions to heal. The question as to whether the complete sterilization of the animals was achieved, we have not yet attempted to answer. This did not, however, seem essential to our first purpose, which was to compare in animals the action of bismuth with that of drugs of known efficacy. That healing of the active lesions did not mean permanent cure is indicated by the course of Rabbit Bi 14. At the time it was given bismuth, this animal had no apparent lesions. It received 2 mg. per kilogram—a dose which healed active lesions in other rabbits—but five weeks later it developed a transitory testicular nodule containing active spirochetes. Observations

on the effect of smaller doses are also summarized in the table. In this series, 2 mg. per kilogram of the tartrobismuthate were curative in the sense stated. Larger doses also gave cures, but half of this amount (1 mg.) gave no definite improvement.

Of the rabbits treated with neo-arsphenamin, those given 6 mg. or more per kilogram were cured. One receiving 3 mg. showed slight temporary improvement with subsequent progression of the lesions. A dose of 1.5 mg. had no perceptible effect. This result is in approximate agreement with Castelli's finding of 11 mg. as the minimal curative dose.

With mercuric salicylate, doses of 15 and 30 mg. caused prompt regression of the lesions but were fatal to the animal. Three and 1.5 mg. had no effect. Rabbit Hg 5, given 6 mg., showed temporary cure with prompt relapse. It appears, then, that only a transitory curative effect is obtainable by single injections of this compound.

It is evident from the results in this series and their comparison with the observations of others that there is wide individual variation in the tolerance of rabbits for these drugs. We cannot yet speak with accuracy of a "maximum tolerated dose," or of the fraction of this which is curative. It seems clear, however, from these experiments that the bismuth salt has a curative effect in amounts well below those which are toxic and that in this respect it is comparable to neo-arsphenamin and definitely superior to mercuric salicylate.

TREATMENT OF HUMAN CASES

As soon as we had confirmed for ourselves the conclusions of Levaditi as to the effectiveness of bismuth in the treatment of syphilis in rabbits, we proceeded to test its action in human cases.

Dosage.—It was attempted to give the dosage recommended by Fournier and Guémot, 0.2 gm., three times a week. With our first preparations, however, the pain at the site of injection was so great that we could not hold patients to this dosage for more than one or two weeks. Later we obtained smoother suspensions which were better tolerated. The discomfort following these is hardly greater than that caused by mercuric salicylate, but it would not be easy to continue injections of an insoluble mercury preparation three times a week over a long period. For inactive cases, we have tried to give only from 0.1 to 0.2 gm. once a week and have been able to hold patients fairly well to this restricted program. From later reports it would seem that bismuth element causes less disturbance than does the quadruple salt, and it is to be hoped that more frequent injections of this can be given and better results obtained. We first selected a few patients with active lesions the course of which was easy to observe.

REPORT OF CASES

CASE 1.—*Primary syphilis.* The patient was a young negro with a chancre on the preputial mucous membrane just back of the corona. The ulcer was 1 cm. in diameter with base and border typically indurated. The left inguinal nodes were about 1 cm. in diameter and hard. Dark-field examination showed numerous spirochetes. The lesion was said to have been present only a week. There was no exanthem or general adenopathy, but the Wassermann test was four plus with alcoholic antigen and two plus with cholesterin antigen. In one week, after three injections of 0.2 gm., the chancre showed slight improvement and the Wassermann test was four plus with alcoholic antigen and 0 with cholesterin antigen. In four weeks, after three more injections of 0.2, 0.1, and 0.1 gm., the lesion was entirely healed, and the Wassermann test was negative. The patient disappeared from observation for the time being, but was seen again after a lapse of three months. There was no sign of recurrence, and the Wassermann test was negative.

CASE 2.—*Primary and secondary syphilis.* A young negro had had a chancre of the lower lip for five weeks (Fig. 7). The entire lip was distended with edema and infiltration, and the cervical nodes were greatly enlarged. There was general adenopathy, a maculo-papular eruption on the trunk, mucous patches on the scrotum, and the patient seemed sick and apathetic. He had

Fig. 7 (Case 2).—*A*, before treatment; *B*, six weeks after treatment; *C*, four months after treatment.

applied a mercury dressing to the lip, and dark-field examination was negative, but the Wassermann test was four plus with both antigens. In one week, after three injections of 0.1, 0.2, and 0.2 gm., the chancre was somewhat smaller, and the exanthem and mucous patches had disappeared. The infiltration of the lip persisted, but a month later, after three more injections of 0.2 gm., the lesion healed, leaving a thin bulging scar without induration. The cervical nodes were still enlarged. The Wassermann test was negative. Five more weekly injections were given, after which the patient abandoned treatment for nine weeks and then returned with a practically normal lip and a negative Wassermann test.

CASE 3.—*Secondary syphilis.*—A young negress had a pronounced papulo-pustular (varioliform) syphilid which had been present for three weeks and which had not improved after one arsphenamin and three mercury injections. The Wassermann test with alcoholic antigen was three plus and with cholesterin antigen, four plus. In two weeks she received six doses of 0.1 gm. As she was very thin, we resorted to injection in the interscapular and deltoid regions, which caused serious discomfort. There was slight improvement in the eruption, and the Wassermann test was one plus with alcoholic antigen, and two plus with cholesterin antigen. She was then put on weekly injections, and in two weeks only a pigmented pattern of the former rash remained; in five weeks

the Wassermann test was negative. After an interval of three months without treatment, no trace remained of the eruption, and the Wassermann test was still negative.

CASE 4.—*Secondary syphilis.* A negress had a pronounced grouped papular (corymbiform) syphiloderm of one week's duration and mucous patches in the vagina. Her Wassermann test was four plus with both antigens. She received

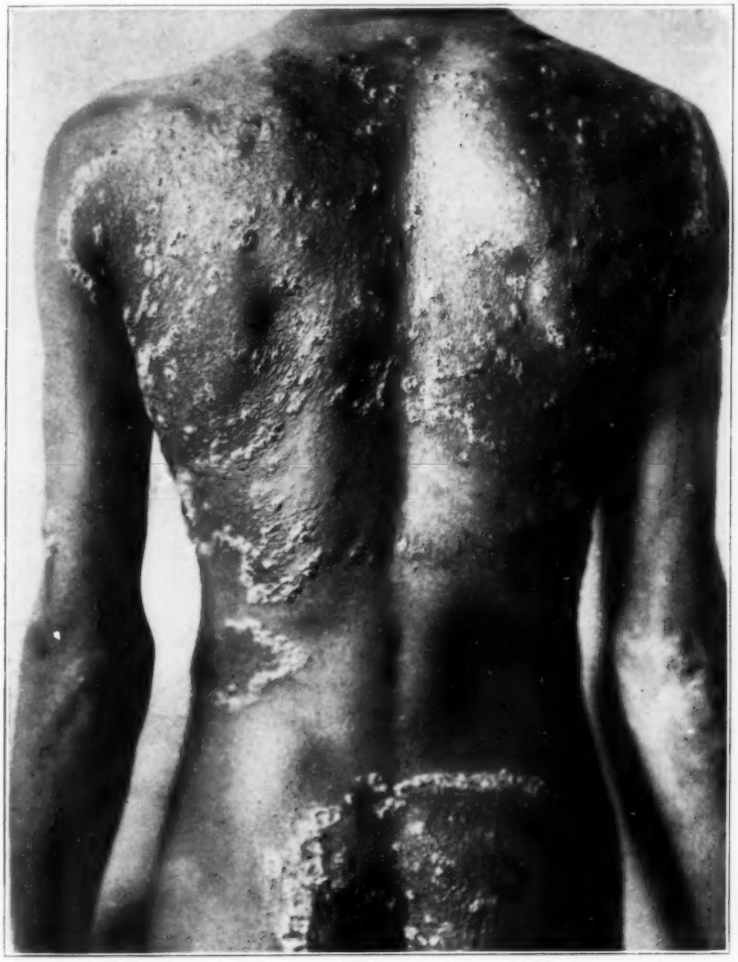

Fig. 8 (Case 5).—Before treatment.

two injections of 0.2 gm. in three days and did not return for four weeks. The eruption had then vanished, her malaise had disappeared, and her blood reaction was negative with alcoholic antigen, and one plus with cholesterin antigen. After this she took weekly treatments with fair regularity for three months during which time tests varied from negative to one plus. Her last Wassermann test, one month after stopping treatment, was negative, and there was no evidence of relapse.

CASE 5.—*Tertiary syphilis.* This patient had appeared in the clinic a year before with a serpiginous syphilid of the shoulder and a four plus Wassermann test. He had refused treatment, and during the year the eruption had spread until it covered most of his trunk (Figs. 8 and 9). His primary infection occurred eight years before, and he had received a few injections of arsphenamin before the outbreak of the tertiary skin lesions. He was given three

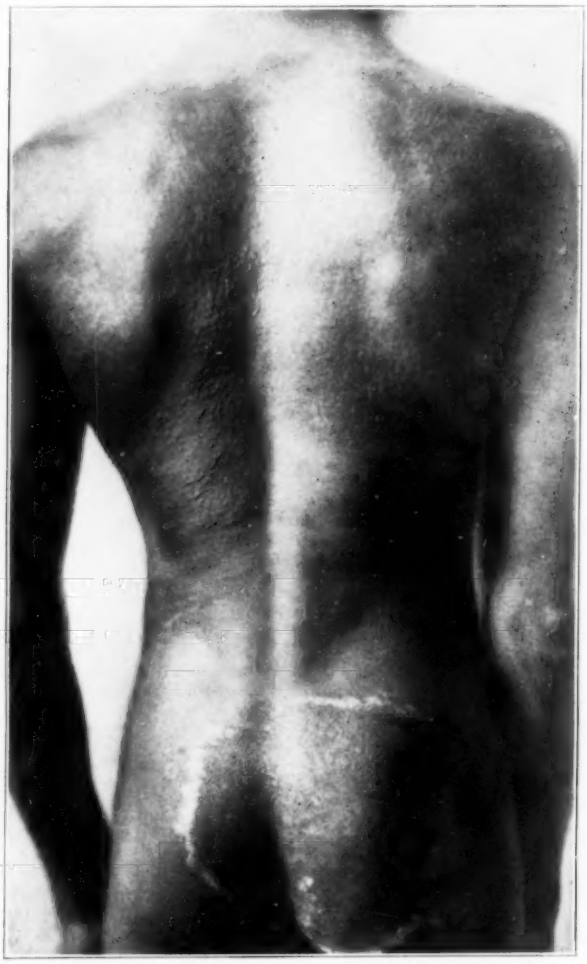

Fig. 9 (Case 5).—Four weeks after treatment.

injections of 0.2 gm. during the first week, followed by three weekly injections of the same amount. At the end of the month, the eruption had practically cleared, leaving only the depigmented pattern of lesions. The blood reaction was still strongly positive. Before treatment, it had been four plus in 0.005 c.c. (one twentieth the standard amount) and after treatment it was four plus in 0.01 c.c. (one tenth the standard amount). We have been unable to trace the patient since.

COMMENT

Other cases with cutaneous lesions responded fairly well to the bismuth injections. Two patients with late periostitis were influenced slowly, the pain persisting for from two to four weeks. One, however, who continued the treatment irregularly for eight months eventually achieved a negative Wassermann reaction.

These cases were sufficient to convince us that in human cutaneous syphilis bismuth has a curative action like that demonstrated in rabbits.

The effects were so similar to those of arsphenamin treatment that it is impossible to form a definite opinion as to the comparative merits of the two drugs from a small series of cases. It seemed to me and to others who watched these patients that Cases 2 and 3 would probably have cleared up more rapidly under intensive arsphenamin treatment, but it is impossible to be certain of this. Surely no other drug in such

TABLE 2.—*Effect of Bismuth Treatment on the Wassermann Reaction in Latent Cases of Syphilis*

Reaction Before Treatment	Number of Injections	Number of Cases	No Improvement	Slight Improvement	Marked Improvement	Marked Improvement with Relapse	Change to Negative
Strongly positive ++++ or +++	4–7	11	2	1	5	3	0
	8–11	7	4	2	1	0	0
	12–15	5	2	1	2	0	0
	16–23	4	1	1	0	1	1
	24–28	4	0	2	0	2	0
Weakly positive	4–22	12	3	0	1	4	4
Total.....	.....	43	12	7	9	10	5

small amounts could have given a more striking effect than was seen in Case 4. As compared with the results obtained with mercury before the introduction of arsphenamin, the cure in all the early cases was rapid. The evidence seems sufficient to indicate that the effect of bismuth in early active syphilis is comparable, though perhaps slightly inferior, to that of arsphenamin, and definitely superior to that of mercury. This conclusion is supported by our animal experiments and by the clinical reports published by others. It applies, of course, only to the immediate effect, as we know nothing so far of the late results.

Concerning the action of bismuth in syphilis of the viscera or of the nervous system, we have nothing to report as yet.

EFFECT ON LATENT SYPHILIS

As we already have in arsphenamin a cure of proved efficiency in early active syphilis, and as there is so far no evidence to indicate that bismuth possesses any great advantage over it except cheapness, it

seemed of more importance to try to learn something of the effect of the new agent on patients with latent syphilis, a class of patients in which the older methods of treatment are so often unsatisfactory. As an indication of the progress in such cases, we are dependent almost solely on the Wassermann reaction, and for the present we can make a preliminary report only on the effect of treatment as measured by this test.

The results so far obtained in thirty-one patients with strongly positive Wassermann reactions (+ + + + or + + +) are shown in

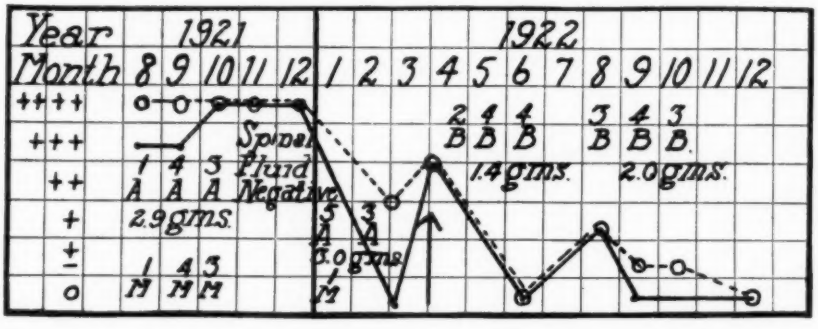

Fig. 10.—Strongly positive Wassermann reaction reduced to negative. In this and the following charts, *A* indicates arsphenamin; *SA*, silver arsphenamin; *M*, mercuric salicylate (gray oil); *B*, sodium potassium tartrobismuthate. The figures indicate the number of injections given. The continuous line indicates the Wassermann reaction with plain alcoholic antigen; the broken line indicates the Wassermann reaction with cholesterin reinforced antigen. The arrow indicates the beginning of bismuth treatment.

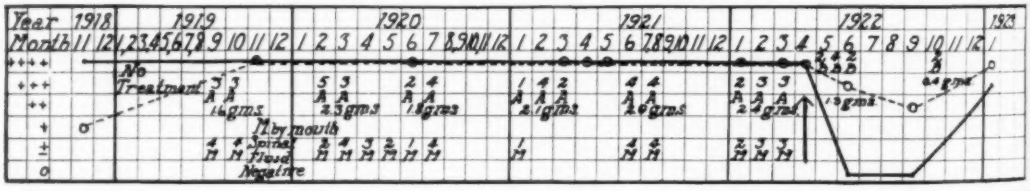

Fig. 11.—Wassermann test uninfluenced by arsphenamin and mercury weakened by bismuth.

Table 2. Of these, twelve had had no previous treatment, seven had had one course of eight injections each of arsphenamin and mercuric salicylate, and twelve had taken two or more such courses. Twelve patients whose Wassermann tests on beginning bismuth treatment were only weakly positive—in most instances as the result of previous treatment—are entered separately. The clearing up of such cases by any method is a long and arduous task, and it is rather soon to expect

decisive results from the bismuth treatment, but in only one have we succeeded in changing a four plus to a negative reaction (Fig. 10), and this result may be only temporary. A number of patients gave a weakened reaction after their first series of bismuth injections and then had a relapse in spite of subsequent treatment. There were, however, several cases in which considerable treatment with arsphenamin and mercury had exerted no apparent influence, but which showed the first break in their series of four plus reactions after taking bismuth (Figs. 11 and 12). There were also one or two that had relapsed to a weak positive after previous treatment who seemed more definitely influenced by bismuth (Fig. 13). It is recognized that such results are

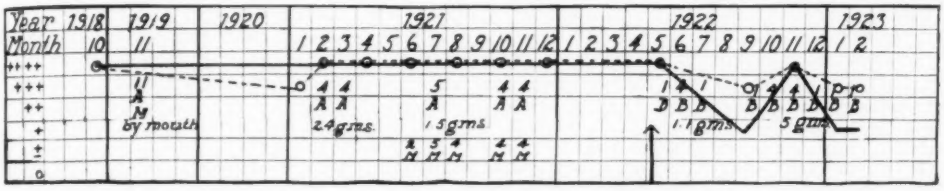

Fig. 12.—Wassermann test uninfluenced by arsphenamin and mercury weakened by bismuth.

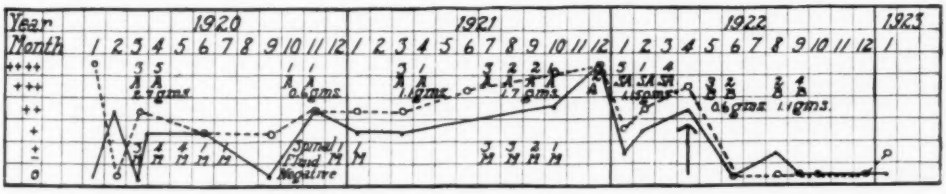

Fig. 13.—Weakly positive Wassermann test reduced to negative after bismuth.

by no means conclusive, but they suggest that bismuth may prove useful in the treatment of some of these resistant cases.

TOXICITY

Of about fifty patients so far treated, two have developed a stomatitis which subsided promptly on interruption of the injections. With the exception of this, we have noted no toxic effects. One patient developed an abscess in the buttock which was probably due to faulty technic, and another showed a swelling from which a clear mucoid fluid was evacuated. A similar reaction was noted by Fournier and Guénot. Frequent examination of the urine has shown no evidence of renal injury. Many of the patients have gained weight and improved in general nutrition under treatment.

CONCLUSIONS

The experiments reported on rabbits show that sodium and potassium tartrobismuthate has marked spirocheticidal power and a curative action on syphilitic lesions in these animals; that in single injection it is about as effective as neo-arsphenamin and more effective than mercuric salicylate.

The observations on early active human cases show that it accomplishes at least a temporary apparent cure.

Its effect on latent cases suggests that it may be useful in the treatment of those which are resistant to other drugs.

These results are in general agreement with those reported by others and indicate that we have in bismuth a new and powerful antisyphilitic agent. There is as yet no reason to suppose that it will replace other drugs, the efficacy of which has been proved by long experience; and at present the treatment of syphilitic patients by bismuth alone is justifiable only in an attempt to appraise its therapeutic value.

Further study of its clinical effect is much needed, but it seems reasonable to hope that better results will be obtained by combined treatment with arsphenamin and bismuth, and probably with mercury also, than by any of these drugs used alone.

LICHEN NITIDUS

H. E. MICHELSON, M.D.
MINNEAPOLIS

Lichen nitidus is now well established as a dermatologic entity. Space is devoted to this disease in the recent editions of dermatologies by Brocq,[1] Joseph,[2] MacLeod,[3] Ormsby,[4] Pusey,[5] Stelwagon[6] and Sutton.[7] Lewandowsky,[8] in his excellent monograph on tuberculosis of the skin, includes lichen nitidus.

One needs only mention the articles of Pinkus[9] and Arndt[10] in Germany, Kyrle[11] in Austria, McDonagh[12] in England and Sutton[13] in America. Occasional cases are demonstrated before the dermatologic societies; Trimble[14] showed a case in New York in 1920; Balban[15] not long ago exhibited such a case before the Vienna Dermatological Society. However, examples of the condition are rare enough to warrant adding a study of a recently observed case to the existing literature.

REPORT OF A CASE

H. E. J., a medical student and hospital intern, married, whose family history was negative, and no near or distant relative of whom had had tuberculosis, said that in the summer of 1919 he spent two months working on a farm.

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2. Joseph, Max: Lehrbuch der Hautkrankheiten, Leipsig, 1922, p. 54.
3. MacLeod, J. M. H.: Diseases of the Skin, London, 1920, p. 744.
4. Ormsby, O. S.: Diseases of the Skin, Philadelphia, Lea & Febiger, 1921, p. 304.
5. Pusey, W. A.: Principles and Practice of Dermatology, New York, D. Appleton and Company, 1917, p. 461.
6. Stelwagon, H. W.: Diseases of the Skin (Gaskill Edition), Philadelphia, W. B. Saunders Company, 1921, p. 218.
7. Sutton, R. L.: Diseases of the Skin, St. Louis, The C. V. Mosby Company, 1921, p. 178.
8. Lewandowsky, F.: Die Tuberculose der Haut, Berlin, 1916, p. 207.
9. Pinkus, F.: Ueber eine neue Knötchen formige Haut eruption, Arch. f. Dermat. u. Syph. **85**:11, 1907.
10. Arndt, G.: Beitrage zur Kenntnis des Lichen nitidus, Dermat. Ztschr. **16**:551, 1909.
11. Kyrle, J.: Beitrage zur Kenntnis des Lichen Nitidus, Arch. f. Dermat. u. Syph. **95**:45, 1909.
12. McDonagh, J. E. R.: Brit. J. Dermat., 1909, p. 339.
13. Sutton, R. L.: Lichen nitidus, J. Cutan. Dis. **28**:597, 1910; Lichen nitidus, Arch. Dermat. & Syph. **2**:1 (July) 1920.
14. Trimble, W. B.: Lichen nitidus, Arch. Dermat. & Syph. **1**:468 (April) 1920; Lichen nitidus, ibid. **1**:721 (June) 1920 (same case).
15. Balban: Lichen nitidus, Dermat. Wchnschr., Nov. 25, 1922, p. 1160.

He harvested barley, and his wrists were often scratched. On returning from the country, he noticed that the palmar surfaces of both wrists were covered with numerous small, slightly elevated, reddish papules. The eruption itched slightly but not sufficiently to cause him to scratch. Scrubbing the wrists caused the papules to redden. A few similar papules appeared over the malar eminences of both cheeks. One per cent. of salicylic acid ointment was applied,

Fig. 1.—View of wrist showing characteristic lesions.

which caused complete disappearance of the eruption on the face; it has not recurred. After violent rubbing, some of the papules on the wrists became very red, even hemorrhagic. The individual papules could be dislocated from their bed by scratching with a sharp scalpel. The seat of the papule would ooze for a short time from several minute points—not from one central point.

The lesions had not reappeared on the face, while the papules on the wrists had remained comparatively stationary. At times the eruption was more

prominent. This was usually after a period of service in the operating room, when the hands were subjected to brisk scrubbing daily. The salicylic acid ointment, although bringing about a disappearance of the papules on the face, had no effect on the eruption on the arms. The Pirquet test was negative.

There was nothing in his personal history, past or present, which in any way had any bearing on his cutaneous condition. A painstaking inquiry concerning tuberculosis revealed no positive evidence. He had gained weight during the past two years, and at no time was he underweight. His wife was well. She had never been pregnant. The Wassermann reaction on the patient's blood was negative.

Examination revealed a well-developed, well-nourished man. His general physical examination was negative. There were no palpable glands, and the mucous membranes were free from abnormalities. The skin condition was confined strictly to the palmar surfaces of both wrists. Here were noted

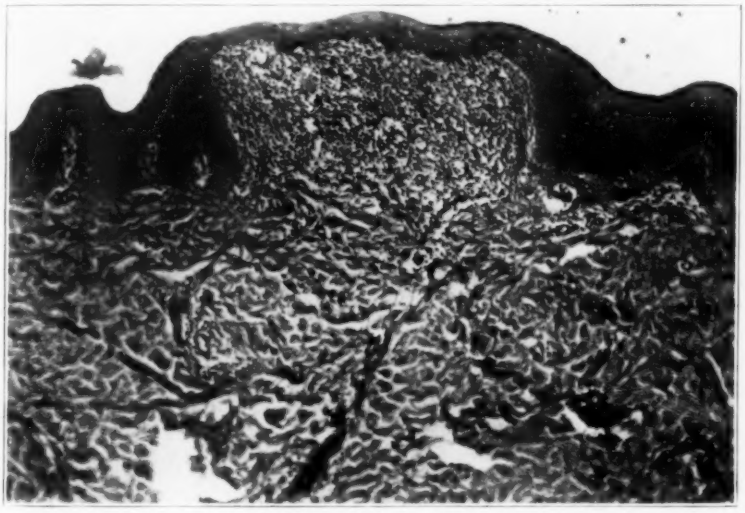

Fig. 2.—Cuboidal shaped mass of infiltrate, with thin walled roof and considerable edema. Low power magnification.

numerous pinhead sized, round or conical, slightly elevated reddish yellow to normal skin colored papules. The papules were distinctly discrete; at no point were they confluent. The summit of the more conical papules seemed to be capped with a minute vesicle. On glass pressure, the papules almost disappeared, remaining as mere grayish opalescent specks. With a tissue needle, the individual lesions could be teased out of their seat, leaving a shallow oozing depression. The papules were palpable, and at no time was softening noted. They were evenly distributed. There was no tendency to grouping or configuration. There was no scaling or verrucous formation, neither was there any secretion or crusting. The papules glistened, but they did not exhibit the silvery sheen of minute psoriasis-papules or even that of lichen planus lesions. No dell formation was noted; in fact, the very center of the papule seemed slightly elevated. Subjectively, the patient was hardly aware of their presence, although they did itch slightly when irritated. He was under observation at varying intervals for three years. During this time the eruption changed little.

DIAGNOSIS

The primary eruption can well be described as the characteristic lesion produced by this disease, for the lesions change little. The condition once seen and identified, especially if examined histologically, leaves such an indelible impression that when the observer sees cases in the future, he will have little difficulty in establishing their identity. The individual lesions in the various cases described in the literature are identical. Only in the number and distribution of the papules do the cases vary. In our case, there were about eighty papules on each wrist. No other part of the integument was involved. Most of the male cases described had lesions on the shaft of the penis and even on the glans. Only three cases have occurred in females. The palmar

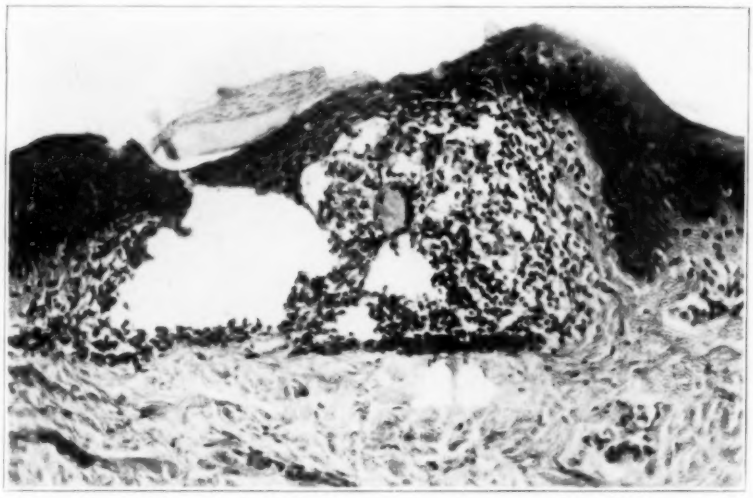

Fig. 3.—Giant cell in infiltrate. Low power magnification.

surfaces of the wrists are also frequently involved. It is worthy of note that only in the female cases was the distribution quite wide. In these three cases, there was a rather general exanthem-like eruption.

The individual lesion is a small papule about the size of the head of a pin—the size is not variable macroscopically. All of the papules in our case were of about the same size. Parounagian [16] exhibited the only case that I have found in which the lesions were reported to be not uniform in size. No biopsy was made, so the diagnosis was not certain. In none of the reported cases were large papules described. The shape of the papule varies a little. Some of them are polygonal in outline, but the majority are round or conical. All are sharply demarcated, and there is no surrounding halo or zone of altered skin.

16. Parounagian, M. B.: Lichen nitidus, Arch. Dermat. & Syph. **3**:89 (Jan.) 1921.

The surface is smooth, with the exception of a few of the lesions, which show a slightly elevated center like a minute superimposed vesicle, but this observation is not substantiated microscopically. There is no exudation, hence no crusting. The color varies from a light flesh color to a pale pink, and a number of the papules, especially at the periphery of the involved areas, are of the same color as the surrounding skin and are barely visible to the naked eye. Macroscopically, there are no follicular papules. There was no tendency to configuration or grouping in the present case; although both arms were involved, the arrangement was not symmetrical. The lesions were most profuse at the center of the wrists, gradually thinning out at the sides and up the forearm.

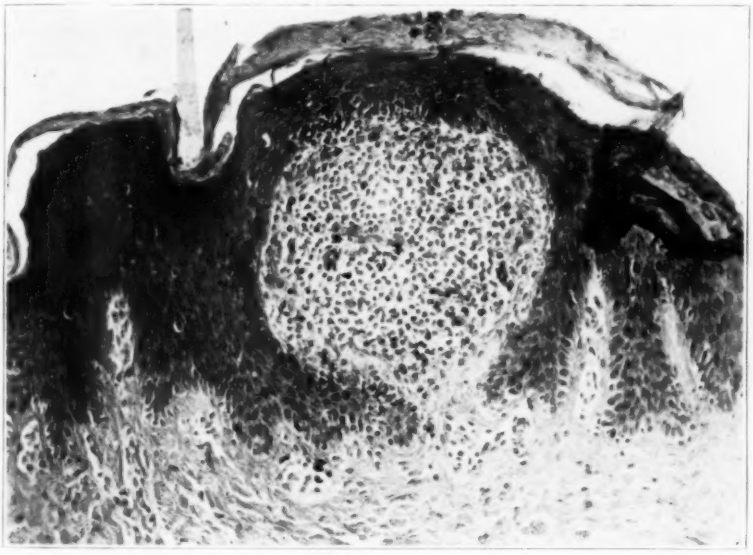

Fig. 4.—Infiltrate mass almost surrounded by elongated rete pegs. Low power magnification.

Under glass pressure, the papules resembled minute lupus nodules, only their color was gray, and they appeared like small grains of sand which were pressed into the skin by the diascope. The individual lesions could be dislocated from their bed with a needle or scalpel. This would leave a minute oozing depression, but small dewdrops of serum did not collect as they do when the scales are removed from a small psoriasis vulgaris papule.

The patient said that, in the interval since he had first noticed the eruption, some papules had disappeared without leaving a trace. There were no scars or pigmentation.

The condition must be clinically differentiated from lichen planus, lichen scrofulosorum and verruca juvenilis.

Lichen planus papules are usually more variable in size. There is a tendency to grouping or formation of figures. The color is lilac or purplish, while, if the glans alone is involved, annular arrangement is the rule, and the color of the papules is of a porcelain white. Arndt observed one case of lichen nitidus in which there were lesions on the buccal mucous membrane, but this is the only case recorded. Lichen planus papules are often delled and have a distinct sheen. Then, too, lichen planus is prone to produce an itching, sometimes quite marked.

Verruca juvenilis differ from lichen nitidus in that the surface of these eruptions is distinctly warty, and they are easily removed with a curet; also their color is usually a light or dirty brown. Their dis-

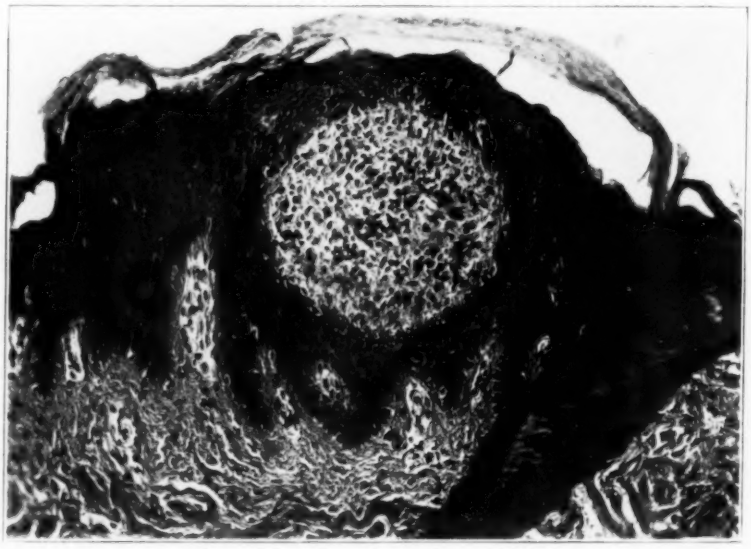

Fig. 5.—Tip of egg shaped infiltrate mass completely surrounded by epidermis. Low power magnification.

tribution is wide, while the number of individual lesions at any one location, as, for instance, the palmar surface of a wrist, is smaller than the number of lichen nitidus lesions, and the individual lesions are less sharply defined and more variable in size.

Lichen scrofulosorum, even of the plane type, usually occurs in children with frank tuberculosis. It always tends to group and is decidedly scaly and perifollicular. Lichen scrofulosorum histologically shows a variable picture. It is seldom of a typical tuberculous structure. The predominating feature is a perifollicular infiltrate containing many lymphocytes, few if any giant cells, and a few epithelioid cells. Caseation rarely, if ever, occurs. In the plane type of lesion which usually occurs in the vicinity of the perifollicular type, the infiltrate is

deeper in the corium than in lichen nitidus. The infiltrate does not penetrate the epidermis. It is not so sharply outlined and is not so uniform.

The relation of this eruption to tuberculosis has concerned all authors. Pinkus mentioned the similarity of the histologic structure. Kyrle made animal inoculations which were negative. His patient gave a marked tuberculin reaction. Lewandowsky [17] observed two patients who later developed frank tuberculosis. He also observed a patient who had a plaque of undoubted lichen scrofulosorum on the arm and lichen nitidus on the penis. Bachrach [18] reported a case occurring in a patient who had pulmonary tuberculosis. He searched for tubercle bacilli but

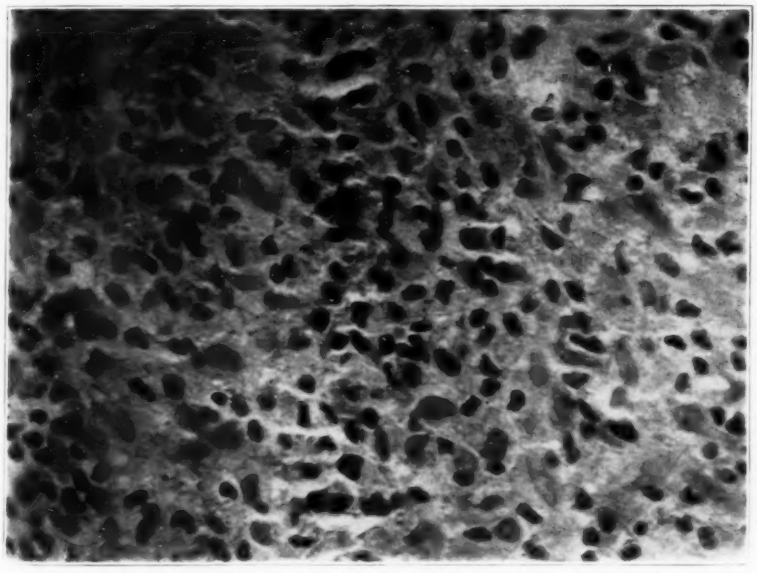

Fig. 6.—Small round cells, fibroblasts and epithelioid cells. High power magnification.

found none. Reines [19] adds his negative findings to those of other observers, but he cites the case observed by Lier,[20] who found acid-fast granules in a microscopic preparation; he also cites the case of Königstein, in which the patient reacted positively to old tuberculin. The fact that lichen nitidus may remain unchanged for years and that the seat of

17. Lewandowsky, F.: Zur Kenntnis des Lichen nitidus, Arch. f. Dermat. u. Syph. **123**:494, 1920.

18. Bachrach: Kasuistischer Beitrag zur Kenntnis des Lichen Nitidus, Dermat. Ztschr. **20**:139, 1913.

19. Reines, S.: Zur Kenntnis eines eigentumlichen Knötchen Ausschlags (Lichen nitidus Pincus), Med. Klin. **6**:1180, 1910.

20. Lier: Protokolle, Wien. Dermat. Gesellsch., 1909 (cited by Reines).

predilection is the shaft of the penis (an area remarkably free from other forms of tuberculosis of the skin) are points against a relationship to tuberculosis. Balban's recent patient reacted positively to old tuberculin.

Zingale,[21] in an extensive review of forty-six cases in the literature and from a study of his own case, finds indications of a relationship to tuberculosis in many cases.

HISTOLOGY

For microscopic examination, an area of skin 4 cm. by 2 cm. was excised from the wrist. The tissue was hardened in formaldehyd and alcohol, serially sectioned (about 400 sections) and stained with hema-

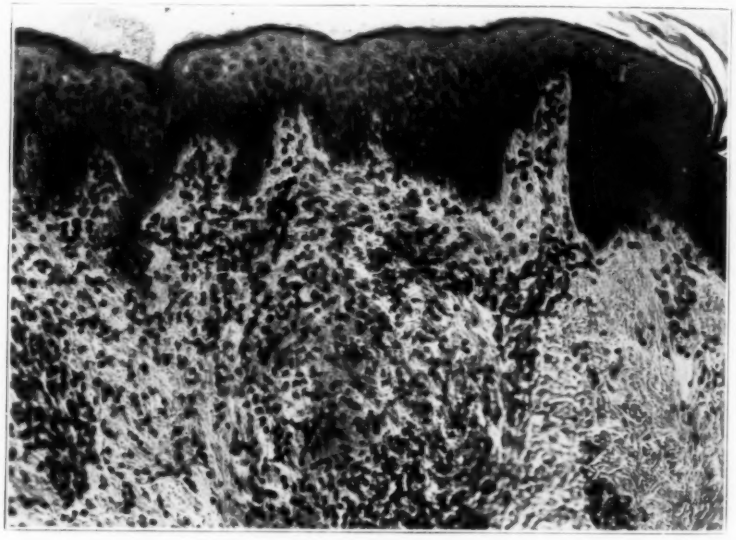

Fig. 7.—Plane type of lichen scrofulosorum. It will be noted that the infiltrate is not so sharply defined, that it is deeper in the corium and that the covering epidermis is unchanged. On studying the complete section, typical perifollicular lesions were easily found adjacent to the plan area.

toxylin eosin, Weigert's elastic tissue stain, and by Ziehl-Nielson's method for tubercle bacilli. Another block was sectioned sagittally (about sixty sections).

From the serial study we ascertained that the shape of the infiltrate mass varied considerably. The majority of the masses were cuboidal with well-rounded corners. Some of the masses were distinctly egg-shaped or Zeppelin shaped with the points completely surrounded by epidermis. From the sagittal sections we noted that the infiltrate mass

21. Zingale, M.: Gior. ital. d. mal. ven. **63**:1099 (Dec.) 1922.

was just about as wide as it was deep, and that the upper surface was flatter than the lower surface. From the lower surface, cords of infiltrate often penetrated deep into the corium.

We found a few lesions in which the sweat duct penetrated the infiltrate, and a few that were about the pilosebaceous follicle, but the majority of the lesions were independent of the ducts.

Under a low power lens, the lesions appeared as a cuboidal mass of closely packed cells lying between the corium and the epidermis, but present more at the expense of the epidermis into which the mass had been pushed, leaving only a thin epidermal covering consisting of three or four layers of the stratum granulosum and a frayed, or in places, thickened stratum corneum, but there was always an epidermal roof present. In preparations in which the infiltrate was cuboidal in shape, the rete pegs were not much altered at the boundaries of the mass; but in the egg-shaped or spherical lesions, especially at the extreme ends, the interpapillary pegs were much elongated, and even fused with the peg from the other side. Professor Kren [22] called my attention to the fact that he had noticed that the epidermal elongations frequently surrounded the infiltrate mass, and he considered this quite characteristic of lichen nitidus.

The lesion itself consisted of closely packed cells, the type and arrangement varying somewhat in individual lesions. There were many deeply staining small round cells, which were irregularly scattered throughout the lesion. Epithelioid and fibroblast cells also were present in considerable numbers. Edematous masses of connective tissue forming a sort of a reticulum ran throughout the mass. Although the infiltrate was dense, the individual cells were distinct, because of an edema which was present in all the sections examined. Giant cells, of the Langerhans type, were rare in our case. Only a few of them were found, and they seemed to be of no importance in their relation to the other cells. No plasma cells were seen nor was caseation noted. The sections stained for organisms revealed no tubercle bacilli or other bacteria.

The histologic findings were in the main identical with the findings in other reported cases.

CONCLUSIONS

In conclusion, we may state that the characteristics of lichen nitidus are:

1. The lesion is a sharply defined granulomatous mass of various shapes made up of small round cells, epithelioid cells, fibroblasts and giant cells in varying numbers.

22. Kren, R. O.: Personal notes.

2. The lesion is always entirely beneath the epidermis.

3. There is no necrosis.

4. Causative organisms have not been identified as yet.

5. Clinically, the lesions more closely resemble minute lichen planus papules.

6. The lesion produced by the plane type of lichen scrofulosorum is the one which most closely resembles lichen nitidus histologically.

7. In our case there was no positive evidence of tuberculosis.

OBSERVATIONS ON DERMATOMYCOSIS IN PORTO RICO

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SAN JUAN, PORTO RICO

For about three years I have been particularly on the alert for cases of dermatomycosis at our skin clinic in San Juan, Porto Rico, and in all dermatoses in which any of the lesions seemed suspicious, no matter what the rest of them looked like, scrapings were taken and examined. The number of positive findings has been surprising, and it is worth while noting a few interesting characteristics which have been found to be common to many of the cases, in the hope that they may throw some light on their diagnosis.

The following histories are taken from my clinic cards.

REPORT OF CASES

CASE 1.—A. D., 17 years old, a high school student in San Juan, reported to my office on Nov. 9, 1921. He complained of an almost generalized eruption from which he had suffered for more than a year. The itching was most annoying, sometimes desperate. He said the eruption had started in the groins. No treatment had given complete relief.

Inspection showed an eruption which covered most of the skin from above the umbilicus to the feet, both at the front and back, and a large portion of the left half of the neck. The individual lesion was a variously-sized circinate patch of hyperemia, with well defined, fairly infiltrated, active borders and a regressive scaly center. The magnifying glass showed that the borders were made up of small papules or vesicopapules. In some places, the lesions had enlarged and coalesced in such a way that extensive regions were covered, acquiring an altogether new aspect, as may be seen in Figures 1, 2 and 3.

The examination of the scrapings under the microscope revealed abundant typical mycelium. Cultures failed.

The diagnosis of dermatomycosis was made, and the possibility of a generalized tinea-cruris was suggested; but we were not able to confirm this theory scientifically on account of the failure of the culture.

Antiparasitic treatment was begun on November 12, and the eruption had completely vanished at the end of two weeks.

CASE 2.—A man, who lived near the town of Rio Piedras, 43 years old, a professor, who was married and had children, came to see me on Sept. 18, 1920, complaining of a generalized skin trouble, with a most intense pruritus compelling him to scratch almost continuously. The disease had lasted fifteen months, and treatment had given no relief.

Examination revealed an extensive patchy eruption which was more generalized than that in Case 1, the only regions actually free being the face and the head. The individual lesion resembled that in Case 1. It consisted of a hyperemic, circinate patch with well defined, infiltrated papulovesicular borders, with a clearer portion at the center. Coalescence occurred, in some places forming larger lesions, but there was a greater tendency to form discrete

patches, so that numerous variously-sized spots could be seen all over the body. There were severe scratch marks all over. The character of the individual patch was so typical of a dermatomycosis that a diagnosis was made at first sight. Scrapings were taken and examined to confirm the diagnosis.

Treatment with Whitfield's ointment was begun on the day of examination, and the eruption disappeared in less than a month.

Fig. 1 (Case 1).—The eruption covers most of the skin from above the umbilicus to the feet, both at the front and back.

COMMENT

There was a striking similarity in general between the eruption in Cases 1 and 2. The isolated lesions corresponded closely in their characteristics; the distribution showed a marked tendency to generalization; and pruritus was a most annoying symptom in both patients.

They had suffered continually in the same way for a long time without relief, while antiparasitic treatment brought about a cure in a few weeks.

CASE 3.—F. M., a Porto Rican by birth, 36 years old, unmarried, came to see me on June 25, 1922. He had lived in the near island of Santo Domingo for the last five years and returned to Porto Rico for the purpose of treatment of

Fig. 2 (Case 1).—In some places the lesions are enlarged and have coalesced in such a way that extensive regions are covered, acquiring an altogether new aspect.

an extensive eruption from which he had suffered for the last sixteen years. He worked as a clerk in a sugar factory; he had a healthy appearance, and there was no pathologic condition in his previous history except this disease.

The eruption was discrete in some places; there were small patches on the back of the thorax, neck, face and eyebrow. But the greater part of it was more diffuse and covered most of the skin from the waist down.

The discrete lesions consisted of groups of small papulovesicles forming patches of varying sizes, with irregular, but definite, rounded borders and some scaling throughout. They were of a bright color and moderate infiltration. Itching was troublesome.

The rest of the affected skin, which was by far the most extensive, (abdomen, buttocks, thighs, legs, etc.) revealed a continuous dermatitis of subacute type with moderate scaliness all over, a fair number of scattered papulovesicles and

Fig. 3 (Case 1).—(An enlarged portion of Figure 2.) The individual lesion is a variously-sized circinate patch of hyperemia with well defined, fairly infiltrated, active borders and a regressive scaly center.

scratch marks here and there. A careful examination revealed, though not clearly, a definite festooned border which limited the eruption upward. Downward the disease faded insensibly into the normal skin in some places. There was maceration between the toes.

In this patient, pruritus was particularly desperate, interfering seriously with his sleep at times. The disease had been present for the last sixteen

years, with alternating exacerbations and remissions, but he had never been free from it during that period.

The typical fungus was found in great numbers, and three weeks of treatment with Whitfield's ointment was sufficient to bring about the complete disappearance of all the lesions.

COMMENT

The cases described are three good examples of a type of dermatomycosis which we have observed in Porto Rico, whose differential features are a tendency to generalization and a marked troublesome pruritus, other symptoms being identical with those of the regular fungous dermatoses. During a long period of observation at the New York Skin and Cancer Hospital and the skin clinic of the Bellevue Hospital, we did not find any dermatomycosis as extensive and pruriginous as those we were dealing with in Porto Rico; and yet we encounter these cases at our clinic with relative frequency. Perhaps the tropical climate exerts some influence on the clinical appearance of this disease.

BIOLOGIC REACTIONS OF ARSPHENAMIN

V. ITS REACTIONS WITH PLASMA PROTEINS AND CERTAIN HYDROPHILIC COLLOIDS AND THE RELATION OF THESE PROCESSES TO THE PHENOMENON OF PROTECTION *

JEAN OLIVER AND ETHEL DOUGLAS

SAN FRANCISCO

It has been found that when arsphenamin is mixed either in vivo or in vitro with blood, marked changes occur in the properties of certain of the proteins of the plasma.[1] The fibrinogen becomes incoagulable to both heat and thrombin. Preliminary experiments have shown that these proteins are in no sense "destroyed," as they may be precipitated by carbon dioxid along with the arsphenamin. These phenomena are similar in nature to the changes in the properties of the globulins when acted on by alkali, and although it has been shown that the hydroxyl ions are not alone responsible for these alterations in our experiments, it may be that arsphenamin reacts in an analogous way with the proteins. If such were the case, a union of protein and arsphenamin would occur. The present study is an examination of this possibility.

Closely related to the main object of this study is the phenomenon of protection against agglutination of red blood cells by arsphenamin, which the proteins exhibit. In a previous communication,[2] we have shown that this protection results from a prevention of the binding of arsphenamin by the red cells and also by preventing the action which electrolytes exert on the absorbed arsphenamin. These are the two essential parts of the process of agglutination by arsphenamin.[3] One general theory of colloid protection holds that there is a union between the active substance and the protecting material, so that the former is no longer able to react with other parts of the system. In

* From the Department of Pathology of the Medical School of Leland Stanford Junior University.

* This investigation has been made with the assistance of a grant from the Committee on Therapeutic Research, Council on Pharmacy and Chemistry, American Medical Association.

1. Oliver, J., and Douglas, E.: Biologic Reactions of Arsphenamin. IV. The Effect of Large Doses on the Coagulability of the Blood, Arch. Dermat & Syph.

2. Oliver, J., and Yamada, S. S.: J. Pharmacol. & Exper. Therap. **19**: 199, 1922.

3. Oliver, J., and Douglas, E.: J. Pharmacol. & Exper. Therap. **19**:187, 1922.

fact, Robertson [4] gives this phenomenon of "masking" as one method of demonstrating protein compounds. Other theories will, however, explain equally well the "protection," so that we have accepted the "compound formation" theory only as a working hypothesis and have examined the processes for further evidence. As other colloids "protect," some of them to a higher degree than protein, certain representatives of this class, gum arabic and egg albumin, have been included in our experiments.

The possibility that arsphenamin may form a compound with plasma proteins has been suggested before. The only experimental evidence with which we are familiar, pointing toward such a conclusion, is that of Young,[5] who showed that in mixtures of arsphenamin and plasma the arsphenamin dialyzed out slowly or not at all. This work was based on Nierenstein's [6] experiments, who previously had shown that atoxyl and other arsenicals behave in this way on dialysis.

METHODS

In all the experiments, unless otherwise noted, the disodium salt of arsphenamin in 2 per cent. aqueous solution was used, prepared by the standard method of the United States Public Health Service. The plasma was obtained by the usual method from rabbits and oxalated to a 1:1,000 sodium oxalate content. The solutions of gum arabic and Merck's egg albumin were prepared with distilled water, filtered and used soon after preparation.

In most of the experiments, the presence of arsphenamin in the precipitates was shown by the quantitative determination of arsenic. This was done by Sanger and Black's modification of the Gutzeit method.[7] Before the actual determination, the organic material was destroyed in the usual way with a mixture of sulphuric acid and nitric acid. In the graphic charts of the experiments, the ordinates are formed by the actual experimental results of the arsenic determinations. The mercuric chlorid strips were pasted on coordinate paper and reduced by photography to one half their actual size.

EXPERIMENTAL

REACTIONS WITH ARSPHENAMIN

In Vivo Experiments.—A rabbit was given 0.27 gm. per kilogram of disodium arsphenamin intravenously. At the end of the injection dyspnea developed, and convulsions and death followed. The blood

4. Robertson, T. B.: The Physical Chemistry of the Proteins, New York, Longmans, Greene & Co., 1918, p. 82.

5. Young, W. J.: Biochem. J. **9**:479, 1915.

6. Nierenstein, M.: Ann. Trop. Med. **2**:249, 323, 1908-1909.

7. Sanger, C. R., and Black, O. F.: J. Soc. Chem. Ind. **26**:1115, 1907.

was collected from the inferior vena cava. The red cells were found agglutinated and the plasma incoagulable. Five cubic centimeters of this blood were centrifuged, the plasma and cells separated, and the latter washed two times with a great excess of 0.9 per cent. salt solution. Both plasma and cells were then treated with strong acid, and the arsenic content determined. Figure 1, *E* and *F*, show the result. The greater part of the arsenic was found in the plasma, but a considerable amount was bound to the agglutinated red cells.

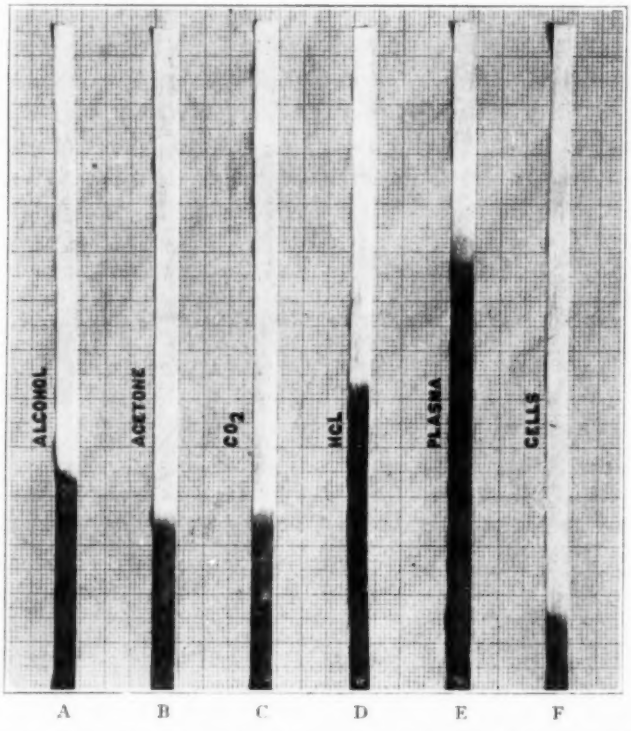

Fig. 1.—Arsphenamin-plasma in vivo. *A-D*, the arsenic content of the proteins of the plasma precipitated by various reagents from the blood of an animal which had received a large intravenous injection of arsphenamin and which died as a result of agglutination of its red cells. *E-F*, the arsenic content of the cells and plasma of 5 c.c. of blood. The charts are photographs of the mercuric chlorid paper strips from the Gutzeit apparatus showing the actual experimental determination of the arsenic, reduced to one half their original size. The arsenic appears as a brownish discoloration.

The plasma from the incoagulable blood was distinctly opalescent and of a greenish yellow tint. On heating to 58 C. for twenty minutes, no precipitation of fibrinogen (globulin) occurred, and the opalescence cleared slightly. Five cubic centimeters were now

diluted to 50 c.c. with distilled water and carbon dioxid passed for ten minutes. A heavy yellow precipitate was caused. This was collected by centrifugalization, washed two times with boiling alcohol [8] and the arsenic content determined. Figure 1, *C* shows the arsenic content of the precipitate. As will be shown later, the arsphenamin may be removed from the precipitate by washing repeatedly in boiling alcohol, leaving the bulky portion of protein behind as a pure white sediment. This is in marked contrast with the yellow precipitate of arsphenamin which results from the passage of carbon dioxid through its solution, as this dissolves completely in the first treatment with alcohol.

The arsphenamin may also be precipitated with the protein by acidification of the yellow opalescent plasma. Three drops of normal hydrochloric acid were added to 5 c.c. of such plasma, and a copious yellow precipitate appeared. This was washed twice with boiling alcohol and its arsenic content determined as shown in Figure 1, *D*.

In the two precipitations detailed above, the precipitant acts on both the arsphenamin and the protein of the plasma. In the case of carbon dioxid, this action is of about equal degree in regard to both the arsphenamin and the globulin, while in the case of hydrochloric acid, the action is in most part on the arsphenamin. If the amount of hydrochloric acid used above is added to normal plasma, it produces little more than an opalescence by a precipitation of the proteins. The greatly increased bulk of the precipitate in the arsphenamin plasma of the previous experiment would therefore seem to indicate that a considerable amount of combined protein is also carried down along with the arsphenamin by the action of the acid.

Results affording a more certain interpretation may be obtained, however, by precipitating the protein by reagents which have no action on the arsphenamin. Acohol is especially adapted for this purpose, as arsphenamin is soluble in it. The method of alcohol precipitation has, moreover, been extensively used for the demonstration of protein compounds with various substances (Simon [9]). Acetone, in which arsphenamin is less soluble but which does not precipitate it in the concentration used in these experiments, may also be used in the same manner.

An equal volume of absolute alcohol was added to 5 c.c. of the opalescent arsphenamin plasma. A heavy yellow precipitate appeared,

8. A standard method of washing was used throughout all the experiments. The precipitate was covered in a test tube with ten times its bulk of absolute alcohol, vigorously shaken and brought to a boil in a water bath. Boiling was continued for about five minutes with repeated shakings and the precipitate collected again by centrifugalization.

9. Simon, F.: Ztschr. f. physiol. Chem. **66**:70, 1910.

which was washed twice in boiling alcohol and its arsenic content determined. A considerable amount of arsenic was found in the precipitated protein (Fig. 1, *A*).

Much the same results were obtained by precipitating the proteins with an equal volume of acetone. The yellow precipitate was found after washing to contain a considerable amount of arsenic (Fig. 1, *B*).

The arsenic of the arsphenamin was therefore bound to the protein which was precipitated by a substance in which arsphenamin is soluble. The instability of this union is shown by the fact that the arsphenamin may be removed by treatment with boiling alcohol, in which it is

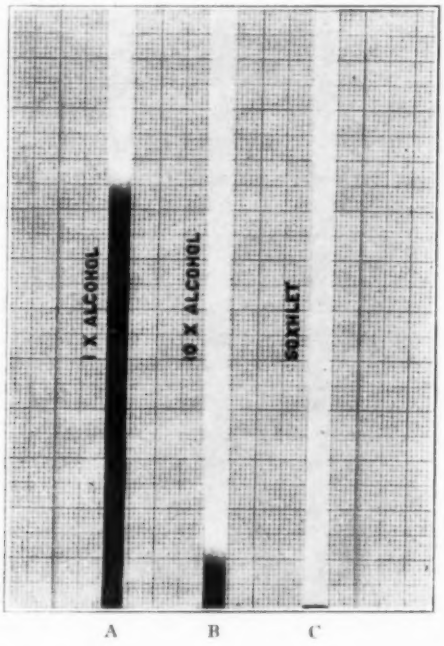

Fig. 2.—Effect of washing on precipitate. *A-C*, the removal of arsenic from the proteins precipitated from the plasma of the experiment portrayed in Figure 1 by extraction with boiling alcohol.

soluble. Three equal portions of arsphenamin plasma were precipitated with equal volumes of absolute alcohol and collected by centrifugalization. The first was quickly rinsed in five volumes of alcohol to remove the adherent supernatant. The second was washed ten times in boiling alcohol, while the third was extracted for thirty hours with boiling alcohol in a Soxhlet apparatus. Figure 2 shows the effect on the arsenic content of the precipitates. The amount of arsenic will therefore depend on the amount of washing, and if this is continued long enough, it practically all may be removed. It is for this reason

that standard conditions of washing were used in all the experiments. The significance of this removal of arsphenamin by a solvent in relation to the nature of the compound formed, and the similar properties which are shown by protein compounds with salts of heavy metals, will be discussed later.

In Vitro Experiments.—The same experiments may be performed with blood or plasma to which arsphenamin has been added in vitro. The findings of these experiments are given briefly, as they are identical with those already detailed. If 0.5 c.c. of arsphenamin is mixed

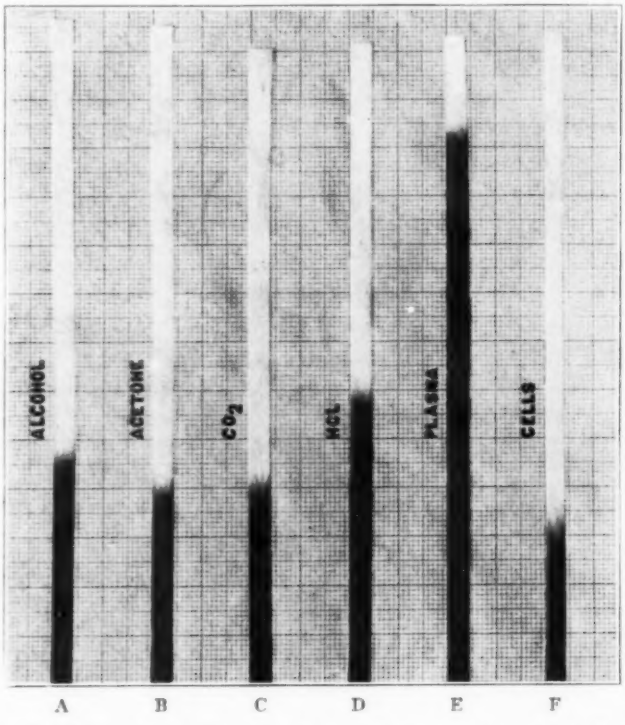

Fig. 3.—Arsphenamin-plasma in vitro. *A-D,* experiment similar to that shown in Figure 1 except that the arsphenamin was added in vitro to normal blood. *E-F,* the partition of arsenic between cells and plasma.

with 5 c.c. of blood, the latter becomes incoagulable, and the plasma has the same yellowish opalescence as is observed after the administration of the drug in vivo. If the cells and plasma are separated, the former are found to have bound considerable arsenic (Fig. 3, *E* and *F*). Heating such plasma to 58 C. for twenty minutes produces no globulin precipitate, but carbon dioxid produces a bulky precipitate of globulin and arsphenamin (Fig. 3, *C*). The addition of 4 drops of normal hydrochloric acid has the same effect (Fig. 3, *D*).

Both alcohol and acetone, which do not precipitate arsphenamin, produce a precipitate of protein which contains considerable arsenic (Fig. 3, *A* and *B*). All of these, if washed sufficiently in boiling alcohol, lose the greater part of their arsenic.

Certain additional experiments may be performed in vitro which are impossible in vivo. A tube containing 5 c.c. of plasma and 0.5 c.c. of arsphenamin was heated to 58 C. for twenty minutes; no precipitate of globulin appeared. When, however, the temperature was raised to boiling, the albumins formed a solid coagulum. Another 5 c.c. of plasma to which 1.5 c.c. of arsphenamin were added showed a marked delay in the development of the coagulum on boiling, and a third portion of 5 c.c. containing 2 c.c. of arsphenamin was still fluid after boiling for twenty minutes. This is in keeping with the general instability of the globulin fraction of the plasma as contrasted with the more stable albumin.

The other additional in vitro experiment bears a relation to the precipitation of protein and arsphenamin by acid. If 0.5 c.c. of a 2 per cent. solution of arsphenamin dihydrochlorid, that is a solution to which no sodium hydroxid has been added, is added to 5 c.c. of plasma, a heavy yellow precipitate results. This yellow precipitate is soluble in an excess of either acid or alkali. After washing twice in boiling alcohol, a considerable amount of arsenic remains bound to the precipitate. This arsenic may be removed completely by extraction with hot alcohol, leaving a large bulk of protein.

The experiments detailed above lend weight to the theory that there is a union between the arsphenamin and the plasma proteins both in vivo and in vitro. At the p_H of the blood, this compound is not completely soluble, as it produces an opalescence of the plasma. In such a plasma the globulins can no longer be coagulated by heat, though the albumins may be. Lowering the p_H by the addition of acid throws down a precipitate in which both arsphenamin and protein are contained. This compound may also be precipitated by alcohol or acetone in which the arsphenamin is soluble.

Many investigators have accepted such evidence as demonstrating the existence of protein compounds with various substances. But the possibility remains that the precipitated protein "adsorbs" the arsphenamin during the process of its precipitation. Such an explanation was given by Dony-Hénault [10] for the occurrence of manganese in alcohol precipitates from colloidal laccase solutions. He found that any salt present in such a solution was carried down in the precipitate of colloid.

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10. Dony-Hénault, O.: Acad. Roy. de Belgique, Bull. de la cl. des sc., 1908, p. 105.

It is difficult to disprove such a possibility in our experiments, and we shall content ourselves for the present with the demonstration that under similar conditions inorganic arsenic is not carried down in any large amount when the proteins are precipitated from plasma. In a later publication we will undertake to demonstrate by other methods that the compound exists before the precipitation occurs.

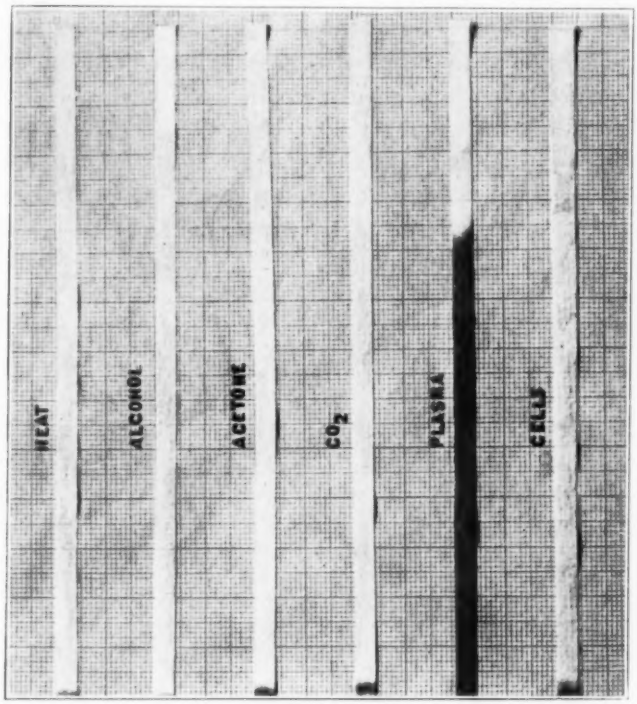

Fig. 4.—Sodium arsenate-plasma in vivo. *A-D*, the arsenic content of the protein precipitates from the plasma of a rabbit which had been given an amount of sodium arsenate containing an equal amount of arsenic as in the experiment illustrated by Figure 1. Comparison with Figure 1 shows that only traces of inorganic arsenic are bound by the proteins. *E-F*, the partition of arsenic between the cells and plasma. Contrast the trace bound by the cells with the large amount of arsphenamin bound in Figure 1.

REACTIONS WITH SODIUM ARSENATE

A sodium arsenate solution was prepared which equaled 2 per cent. disodium arsphenamin in its arsenic content. With this solution, the experiments detailed above were repeated, and the various precipitates tested for the presence of arsenic.

In Vivo Experiments.—A rabbit was given sodium arsenic solution in a dose containing as much arsenic as was given in the form of

arsphenamin in the previous experiments. There was no observable reaction on the part of the rabbit. Blood drawn from the ear vein clotted in the normal time and manner. The animal was then bled into sodium oxalate solution. Five cubic centimeters of this blood were centrifuged, the cells removed and washed twice in 0.9 per cent. saline and the arsenic content of them and of the supernatant plasma determined. Figure 4, *E* and *F*, show that practically all the arsenic was in the plasma and that only a trace was bound by the cells.

Five cubic centimeters of the clear plasma were heated to 58 C. for twenty minutes. A heavy precipitate of globulins appeared. This was washed twice in hot alcohol, in which sodium arsenate is only slightly soluble. The determination of arsenic showed only the faintest trace (Fig. 4 *A*). Similarly, 5 c.c. portions of plasma in which the proteins were thrown down by carbon dioxid, alcohol and acetone, washed in boiling alcohol and tested for arsenic, showed only the faintest traces (Fig. 4, *B*, *C* and *D*). Acidification with 4 drops of normal hydrochloric acid produced no frank precipitate, but only an opalescence, so that no analogous experiment to that done with arsphenamin plasma and acid could be performed.

The administration of a considerably larger amount of arsenic in the form of sodium arsenate produces no change in the experimental results. The experiment described above was repeated, using six times the amount of sodium arsenate. No immediate reaction occurred in the animal, its blood coagulated normally, heat threw down the globulins and no greater traces of arsenic were found in various protein precipitates than in the experiment just described.

In Vitro Experiments.—The results of the in vitro experiments may be briefly summarized, since blood treated with sodium arsenate in the test tube gave identical reactions with the blood of an animal which had received an intravenous injection of it. The blood clotted promptly, the arsenic was not fixed to the cells but was contained only in the plasma, the globulins were coagulated by heating to 58 C., and precipitates of the proteins of such a plasma by carbon dioxid, alcohol and acetone showed only traces of bound arsenic (Fig. 5, *A*, *B*, *C*, *D*, *E* and *F*).

The evidence accumulated thus far may be summarized as indicating that a union of arsphenamin and the proteins of the plasma occurs under physiologic conditions of acidity (p_H 7.5), which results in an alteration of the properties of certain of these. The arsphenamin is also bound to the red cells when it is present in sufficient concentration to cause the agglutination of these elements. Under the same conditions, no evidence was found that would indicate that inorganic

arsenic is bound by either plasma protein or red cells. The reaction between the arsphenamin and the plasma or cells is therefore specific to a greater degree than the criticism of Dony-Hénault would indicate.

INFLUENCE OF P_H ON THE REACTIONS IN PLASMA

In former studies on the effect of arsphenamin on agglutination of red cells and on the coagulability of the blood, it was found that the p_H of the medium in which the reaction occurred influenced the course of the reaction to a decided degree. And it is well known that the

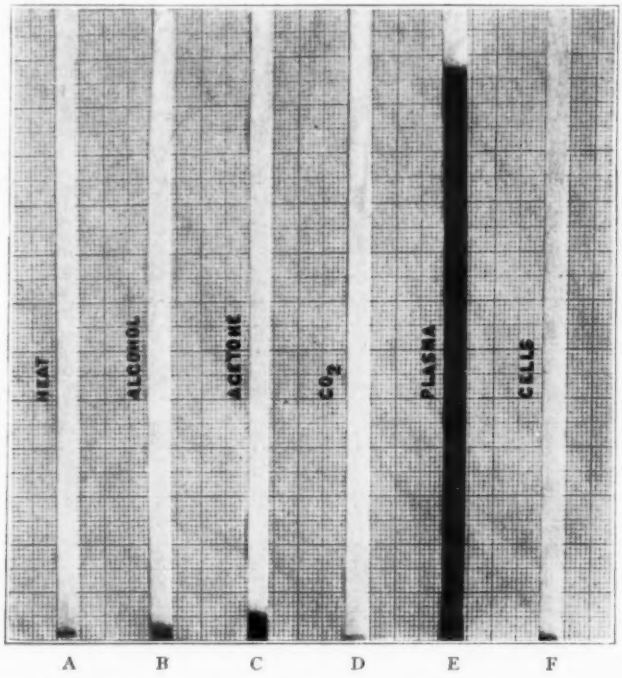

Fig. 5.—Sodium arsenate-plasma in vitro. *A-F*, the arsenic content of the protein precipitates, plasma and cells of blood to which sodium arsenate was added in vitro. The findings are similar to those shown in Figure 4, but in marked contrast to those of Figure 3.

formation of compounds between amphoteric colloids and various substances is greatly altered by variations in acidity. Loeb's [11] studies of gelatin compounds with either the cation or the anion of salts depending on the reaction of the medium in relation to the isoelectric point of the colloid, may be cited as an example of the importance of this factor. At the present time we intend to study this point

11. Loeb, J.: J. Gen. Physiol. **1**:39, 1918-1919.

only briefly, and hope to return to a general consideration of the influence of hydrogen and hydroxyl ions on the reactions of arsphenamin in all the phases that we have thus far studied.

The experiments were performed by using 2 per cent. arsphenamin solution and an arsenic-equivalent solution of sodium arsenate. Two series of four tubes were prepared, each containing 5 c.c. of plasma. The acidity of each series was regulated by the addition of hydrochloric acid and sodium hydroxid so that the final p_H in them was

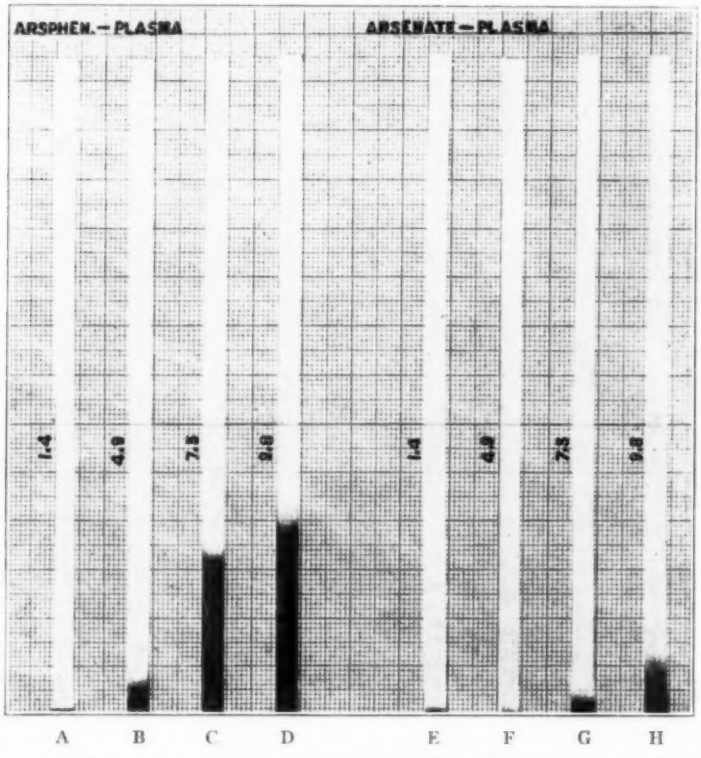

Fig. 6.—Effect of hydrogen-ion concentration. The effect of the H-ion concentration on the arsenic content of the proteins precipitated by absolute alcohol from plasma to which arsphenamin had been added (*A-D*) and to which an arsenic-equivalent solution of sodium arsenate had been added (*E-H*). Note the contrast between the amounts of the two substances bound at the physiologic p_H 7.5.

1.4, 4.9, 7.5 and 9.8. To one series was added 0.5 c.c. of arsphenamin and to the other 0.5 c.c. sodium arsenate solution. The addition of these two reagents produced no observable change in the p_H of the mixtures, as the buffer substances of the plasma were capable of controlling such a variation. An equal volume of absolute alcohol was

added to each tube of the two series; arsphenamin plasma and sodium arsenate plasma. The resulting precipitates were washed in the usual way in boiling alcohol, and the arsenic content determined. Figure 6 represents the results. Arsphenamin was not bound by the plasma at a p_H of 1.4 and only slightly bound at 4.9. At 7.5 (physiologic reaction) a large amount was bound, and there was some increase in this amount at 9.8 (Fig. 6, *A, B, C* and *D*). Sodium arsenate was not bound at 1.4 or 4.9 and only a trace at 7.5 (physiologic reaction). At 9.8 a small amount was found in the precipitate (Fig. 6, *E, F, G* and *H*).

COMMENT

The experiment shows that there is an increasing degree of binding by plasma of both arsphenamin and sodium arsenate as the alkalinity of the medium increases. It also shows that the binding of arsphenamin is not due to the alkalinity of the disodium salt alone, as under the same degree of hydroxyl ion concentration a relatively large amount of arsphenamin was bound as compared with the small amount of inorganic arsenic.

EXPERIMENTS ON THE RELATION OF BINDING TO PROTECTION

The final experiments were carried out to determine whether binding of arsphenamin by plasma proteins could be considered the cause of the protection which plasma affords against agglutination of the red blood cells by arsphenamin. It has been shown that a similar protection is afforded by other colloids,[2] so that it must first be determined whether these substances also bind arsphenamin.

In these experiments the method of alcohol and acetone precipitation of the colloid solutions containing arsphenamin and sodium arsenate in the same proportions as the previous experiments with plasma was used. *A priori*, it is likely that if compounds of colloid and arsphenamin occur, the binding of the arsphenamin will vary with the H-ion concentration of the medium, so that this point was determined in the same experiment.

Two series of four tubes each containing 5 c.c. of a 3 per cent. gum arabic solution were prepared, and the reaction adjusted by the addition of hydrochloric acid or sodium hydroxid to p_H 1.4, 5, 8 and 9.8. The gum solution as prepared with distilled water normally has a p_H of from 4.5 to 5. To one of the series was added 0.5 c.c. of a 2 per cent. arsphenamin solution and to the other a similar amount of arsenic equivalent sodium arsenate solution. Equal volumes of absolute alcohol were then added, and, to aid the process of flocculation, a few drops of electrolyte in the form of potassium chlorid solution. These precipitates were then washed twice in boiling alcohol in the usual

manner, and their arsenic content determined (Fig. 7). It will be observed that the gum arabic binds the arsphenamin in larger amounts as the alkalinity of the solution increases. In comparison with the binding by plasma proteins (Fig. 6, *A, B, C* and *D*), it will be noticed that greater amounts are bound at all degrees of alkalinity by the gum, and also that it binds a considerable amount at p_H 1.4, at which figure none was bound by plasma. The decrease in the amount bound at the

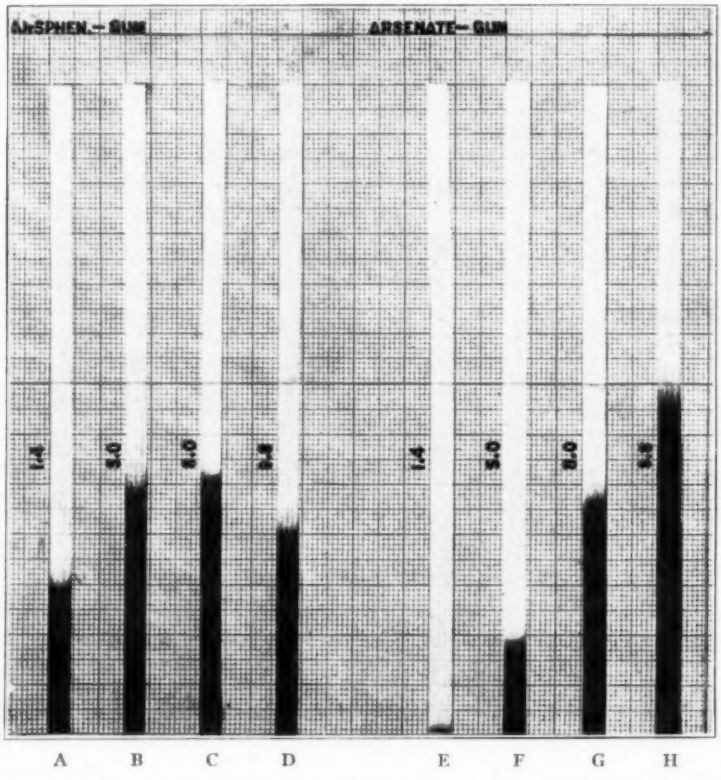

Fig. 7.—Effect of hydrogen-ion concentration. A similar experiment showing the arsenic content of gum arabic precipitated from its solution which contained arsphenamin (*A-D*) and an arsenic equivalent amount of sodium arsenate (*E-H*).

high alkalinity was observed in several experiments. Sodium arsenate is also bound to a greater degree than by plasma proteins (Fig. 6, *E, F, G* and *H*), but to a lesser degree than is arsphenamin, except at high degrees of alkalinity. Another variation with the binding of sodium arsenate by plasma is that whereas the latter does not bind at its "normal" p_H (7.5), gum arabic does (p_H 5).

Similar experiments were performed with a 3 per cent. solution of Merck's egg albumin. The results may be summarized as follows:

Arsphenamin is "bound" to a lesser degree than by plasma proteins. The reaction increases with alkalinity. Sodium arsenate was "bound" to a lesser degree than arsphenamin, and a small amount at the normal p_H (6).

COMMENT

It is therefore evident that these other colloids, which exhibit the phenomenon of protection in common with the plasma proteins, also "bind" arsphenamin in a similar manner as do these substances.

In the following experiments a direct comparison was made between the relative binding of arsphenamin by these various substances and their relative protecting abilities, for it is known that the latter properties vary considerably.[2]

Plasma was diluted with 0.9 sodium chlorid solution until its protein content was approximately 3 per cent. Gum arabic and egg

TABLE 1.—RESULTS OF EXPERIMENTS WITH COLLOIDS EXHIBITING PROTECTION *

	C	1:2	1:4	1:8	1:16	1:32	Gm. Colloid Which Fail to Protect	Reciprocal	Value of Reciprocal	Value of Arsenic Bound
Gum.....	0	0	0	0	±	+	0.0003	3,333	4	3.9
Plasma.....	0	0	0	±	+	C	0.0006	1,666	2	1.5
Albumin.....	0	0	±	+	C	C	0.0012	833	1	1.0

* 0.25 c.c. colloid dilution + 0.25 c.c. arsphenamin solution + 0.25 c.c. red cell suspension.

albumin also were prepared in 3 per cent. solution. With these solutions dilutions were made and added in agglutination tubes to a mixture of washed red blood cell suspension and arsphenamin. The amount of the latter was the optimum agglutinating dose. After incubation at 37 C. for one hour the readings were made. The degree of protection is shown in Table 1.

The relative protective power of the three substances is shown in the tenth column of the table. Gum arabic protects four times as effectively as albumin, and plasma twice as well.

Five tenths cubic centimeters of arsphenamin were added to 5 c.c. of the solutions used in this experiment. The colloids were precipitated by absolute alcohol, washed twice in boiling alcohol and their arsenic content determined. Figure 8 shows the result. The relative values of these amounts is given in column 11 of Table 1. It will be noted that there is a close parallelism between the ability of the substances to bind arsphenamin and their protective power.

Protection and binding are evidently closely related. Can it be demonstrated that this relation is due to the protection being the result of the binding? The following experiment demonstrates that this is the case.

Five cubic centimeters of 0.03 per cent. arsphenamin in isotonic sucrose solution were added to 5 c.c. of 25 per cent. suspension of red cells and a final 5 c.c. of isotonic sucrose solution added. Another tube contained 5 c.c. of the same arsphenamin solution and 5 c.c. of cell suspension, and in addition 5 c.c. of plasma. Both tubes were incubated for two hours at 37 C. The cells in the tube without plasma

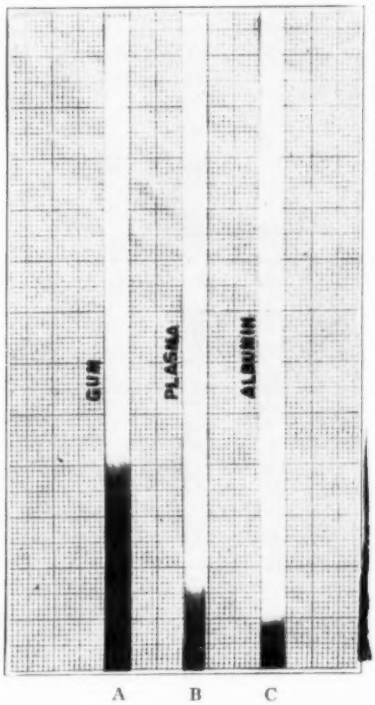

Fig. 8.—Binding and protection. The arsenic content of precipitates from 3 per cent. solutions of gum arabic, plasma and Merck's egg albumin containing equal amounts of arsphenamin. The arsenic content decreases in the proportion of 4, 1.5 and 1. Table 1 shows that the protection against agglutination by arsphenamin afforded by these substances decreases in a corresponding degree.

agglutinated, while the cells in the tube which contained plasma were protected against this process. The cells in both tubes were removed by centrifugalization, washed twice in isotonic sucrose solution and the washings added to the original supernatant fluids. The proteins of the supernatant containing the plasma were now precipitated with

absolute alcohol and washed twice in the usual manner in boiling alcohol. The cells from both tubes, the supernatant of the agglutinated tube and the precipitated protein from the tube which had been protected by plasma, were now all tested for arsenic. Figure 9 shows the results. The agglutinated cells of the unprotected tube had bound a large amount of arsphenamin (Fig. 9, 1), and some arsphenamin remained free in the supernatant fluid (Fig. 9, 2). In the tube in which no agglutination had occurred, due to the protection by the plasma present, the unagglutinated cells had bound no arsphenamin (Fig. 9, 3). The arsphenamin was found bound to the proteins of this protecting plasma (Fig. 9, 4).

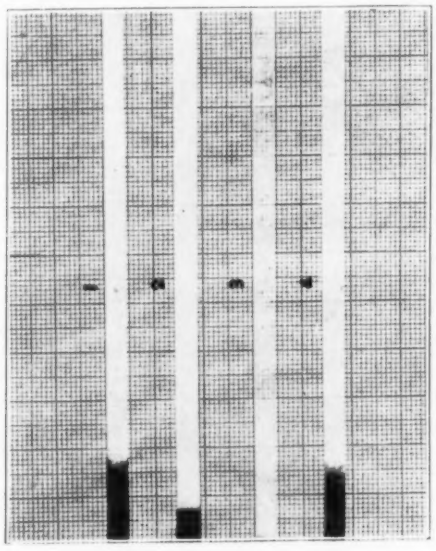

Fig. 9.—Method of protection. The method by which plasma protects its red cells from agglutination by arsphenamin. 1-2, a suspension of red cells, free of plasma, to which arsphenamin was added with a resulting agglutination of the cells. Arsenic is found in the plasma (1) and also bound to the agglutinated cells (2). 3-4, a similar suspension of red cells but containing plasma, to which arsphenamin was added, and in which no agglutination occurred due to protection. The protected unagglutinated cells are free of arsenic (3), but the proteins precipitated from the protecting plasma contain it (4).

Protection in this experiment was evidently due to a union of the arsphenamin with the proteins of the protecting plasma instead of with the red cells of the suspension. This union with the cells has been shown to be the first step in the process of agglutination of them by this substance.[3]

If reference is made to Figure 1, *E* and *F*, it will be recalled that when arsphenamin is injected into an animal in such an amount that death results from in vivo agglutination of its red cells, a considerable amount of the arsphenamin is found bound to the agglutinated cells. It may be asked whether the lack of agglutination following therapeutic doses is due to a protection by the plasma proteins. The following experiment shows this to be true.

One and one-half cubic centimeters of 2 per cent. arsphenamin solution was injected intravenously into a 1,500 gm. rabbit. This equals 0.02 gm. per kilogram, approximately twice the usual therapeutic dose. Following the injection the animal was bled into oxalate.

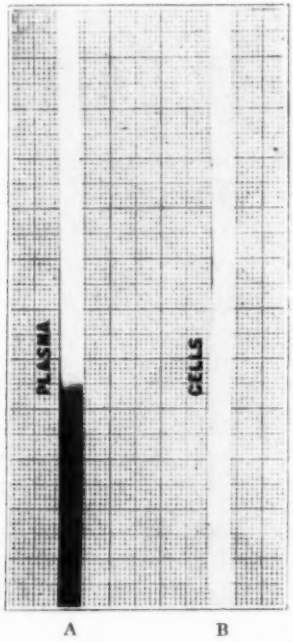

Fig. 10.—Protection in vivo. Showing protection of red cells in vivo by the plasma of the blood when small doses of arsphenamin are given intravenously. The arsenic is found only in the plasma, bound to the proteins, while the red cells are free from it. Contrast with Figure 1, *E-F*, in which such a large dose of arsphenamin was given that the proteins were "saturated" and the excess arsphenamin was bound by the red cells with a resulting agglutination of them, and death of the animal.

There was no agglutination of the red cells. Ten cubic centimeters of this blood were separated into cells and plasma by centrifugalization. The cells were washed twice with 0.9 per cent. physiologic sodium chlorid solution, and the washings added to the supernatant plasma. The arsenic content was then determined in both cells and plasma.

Figure 10 shows that the plasma contained all the arsphenamin where the previous experiment showed that it was fixed to the proteins, and that the protected red cells were entirely free of arsenic.

Protection in vivo from therapeutic doses is therefore due to a union of the arsphenamin with the plasma proteins instead of with the red blood cells.

It will be remembered that it has been demonstrated that the coagulating properties of the globulins of the plasma are affected by low concentrations of arsphenamin, while a considerable concentration is necessary to alter these properties of the albumins. Does the relative degree of these changes bear any relation to the degree of binding of arsphenamin by the two proteins?

If the change which is produced by arsphenamin in the coagulating properties of the two substances is the result of a union of the arsphenamin with the protein bodies, since protection results from

TABLE 2.—RESULTS OF EXPERIMENT *

	1:2	1:4	1:8	1:16	1:32	1:64	1:128	Colloid Dilution	Arsphenamin Solution
Whole plasma†	0	0	0	±	C	C	C	0	C
Globulin fraction	0	0	0	0	+	C	C	0	
Albumin fraction	0	−	C	C	C	C	C	0	

* 0.25 c.c. colloid dilution + 0.25 c.c. arsphenamin solution + 0.25 c.c. red cell suspension.
† The original sample of plasma had been kept in the icebox during the preparation of the fractions and had precipitated slightly. This doubtless explains its lower protective power as compared with the globulin fraction.

this union, that protein whose properties are most affected should protect to a greater degree. If globulin should protect against agglutination more markedly than does albumin, we could infer that it unites with arsphenamin to a greater degree than does albumin, and it would be highly likely that for this reason the anticoagulating effect of the arsphenamin is more pronounced in its case. This point was investigated in the following way:

Fifteen cubic centimeters of plasma were half saturated with ammonium sulphate and the precipitate removed. The clear supernatant was precipitated by saturation with finely powdered ammonium sulphate. Both precipitates were dissolved in 15 c.c. of distilled water and dialyzed to remove the excess salts. The globulins precipitated during this procedure and were redissolved by adding a small amount of sodium chlorid. The two preparations now contained the globulins and the albumins of the plasma in their original concentration. Dilutions of these two preparations were made, as well as a series of

dilutions of the original plasma. Portions of these were added in agglutinating tubes to arsphenamin solution and to a suspension of red cells and incubated at 37 C. for one hour. Table 2 shows the results.

This experiment shows the relative protective value of the proteins of the plasma. The globulins are the bodies most actively concerned in the process, for they bind arsphenamin to a greater degree than do the albumins, and in the whole plasma they first react with arsphenamin, forming compounds which do not coagulate on heating. A further addition of arsphenamin has been shown to be required before the union with this excess arsphenamin affects the coagulability of the albumins.

SUMMARY AND DISCUSSION

The globulins of the plasma are rendered heat incoagulable by the addition of arsphenamin. The precipitate of these incoagulable proteins by a reagent in which arsphenamin is soluble, such as alcohol, contains the latter substance bound to the protein. It may be removed from the proteins by prolonged extraction in hot alcohol. Similarly an increase in the hydrogen-ion concentration will precipitate out a combination of arsphenamin and protein, or the same result may be accomplished by the use of "acid arsphenamin" instead of the disodium salt. The amount of arsphenamin bound by the protein increases with the alkalinity of the medium in which the reaction occurs. None of these reactions occurs in normal plasma to which inorganic arsenate has been added. The precipitated proteins do not bind this arsenic at the normal p_H of the blood, though at high degrees of alkalinity, some is bound.

These same reactions occur in vivo when arsphenamin or sodium arsenate is injected intravenously. The proteins of the plasma and the cells of the blood bind arsphenamin, but not arsenates.

Other hydrophilic colloids bind arsphenamin. Gum arabic binds both arsphenamin and arsenate to a greater degree than do the plasma proteins, while egg albumin is less active in this regard. The p_H affects the degree of binding in a similar manner as was observed in binding by plasma proteins.

Binding of arsphenamin by these hydrophilic colloids and the protection against agglutination of the red blood cells by arsphenamin are parallel processes. The parallelism is due to the protection being a result of the binding of the arsphenamin by the colloid, thus preventing a union of the arsphenamin with the red cells, a process which is necessary for the occurrence of agglutination. The globulin fraction of the plasma proteins protects against agglutination to a greater degree than the albumin fraction. Since protection is due to binding, it may be inferred that the globulin binds the arsphenamin to a greater degree, and this will explain the changes in its heat coagulation properties by concentrations of arsphenamin which are too low to affect the properties of the albumins.

When arsphenamin is administered in vivo, a union occurs between this substance and the plasma proteins, in particular the globulins. Little, if any, arsphenamin reaches the red cells, and they are in this way protected from the agglutinating action of arsphenamin. If a large enough dose is given, however, the protecting proteins may be "saturated" and free arsphenamin is bound by the cells. Agglutination of them may result and an acute reaction followed by death occurs.[12] The blood of such an animal does not coagulate, as the arsphenamin fibrinogen complex is not coagulated by thrombin.[1]

There is a striking similarity between the action of alkali on the coagulation of protein by heat and the action of arsphenamin. The explanation of the mechanism of the action of the alkali as given by Pauli [13] and Erb [14] will also explain the lack of heat coagulation which arsphenamin causes. According to these investigators, if the protein is heated in alkaline solution, no coagulation results, because the protein, acting as an acid, has formed a soluble salt with the metal ion of the alkali. In acid solutions the same lack of coagulation by heat is due to the proteins forming a similarly soluble salt with the acid radical ions. At a certain range of p_H, however, these salts are insoluble and appear as a precipitate. Pauli [13] has shown that such soluble salts are formed with most of the bases, potassium, sodium, lithium, and the ammonium ion (NH_4^+). Of special interest to us is the demonstration by Spiro [15] that organic bases have the same property. Cholin, pyridin, anilin, orthotoluidin and even such weakly basic substances as urea and urethane form soluble salts with protein and so hold it in solution when heated.

To this last list may be added arsphenamin. The "salt" which it forms with plasma proteins is soluble at certain degrees of alkalinity, and the amount formed increases with the alkalinity of the medium. Heating such a plasma produces no flocculation if the p_H is one at which the compound is soluble. At the p_H of the blood it causes an opalescence, and if the alkalinity is still further lowered by the addition of acid, the compound is precipitated. The precipitated compound may be dissolved in either acid or alkali. Previous experiments have also shown that under the same conditions this compound of arsphenamin and fibrinogen (globulin) is not coagulated by thrombin.[1]

Our experiments afford no evidence as to the nature of the complex formed between the arsphenamin and the colloids. For this reason we have used the general terms "compound" for the substance

12. Oliver, J., and Yamada, S. S.: J. Pharmacol. & Exper. Therap. **19,** 393, 1922.

13. Pauli, W.: Beitr. z. chem. Phys. u. Path. **5**:27, 1904.

14. Erb, W.: Ztschr. f. Biol. **41**:309, 1901.

15. Spiro, K.: Ztschr. f. physiol. Chem. **30**:182, 1900.

formed, and "binding" or "union" for the process. No field of biochemistry is more disputed than that which is concerned with the nature of protein compounds with various substances. "Adsorption" and "chemical" union, are held by the two separate schools best to explain the nature of the substance formed. To many, a complex one of whose elements may be removed by the action of a simple solvent, would seem best explained by the assumption that the union is a loose one due to capillary attraction. Such a physical "adsorption" might explain the union of arsphenamin and protein. But such evidence is not accepted by those who hold that these compounds are "true" chemical compounds. The criticism of Robertson [16] on these matters may be consulted by the reader.

Whatever the nature of the arsphenamin protein compound, its reaction with a solvent of one of its fractions is the same as that shown by the compounds of protein with salts of heavy metals. Galeotti [17] has shown that the silver content of the compound formed in the precipitation of protein by silver nitrate varies with the amount of washing to which the precipitate has been subjected.

The compounds of arsphenamin and protein described in this study are doubtless the same formations which have been studied in vitro by various observers as "arsphenamin precipitates." Joseph [18] has shown that "acid-arsphenamin" is precipitated in the blood stream, and Danysz [19] has claimed that the in vivo formation of such precipitates would account for acute reactions following the injection of alkaline arsphenamin. Schamberg and Kolmer [20] have pointed out, however, the importance of the p_H of the medium in which the reaction occurs, and have shown that with disodium arsphenamin no "precipitate" forms in serum. Much of the conflicting evidence concerning the occurrence of these "arsphenamin precipitates" in vitro is probably due to a lack of control of the p_H, either by using insufficiently neutralized arsphenamin solution or by allowing carbon dioxid absorption from the air by the serum to alter its original neutrality.

CONCLUSIONS

1. The plasma proteins, especially the globulins, form compounds with arsphenamin both in vitro and in vivo. The arsphenamin content of these compounds varies with the H-ion concentration.

16. Robertson, T. B.: J. Biol. Chem. **4**:35, 1908.
17. Galeotti, G.: Ztschr. f. physiol. Chem. **40**:492, 1904.
18. Joseph, D. R.: J. Exper. Med. **14**:83, 1911.
19. Danysz, J.: Ann. de l'Inst. Pasteur **31**:114, 483, 1917.
20. Schamberg, J. F.; Kolmer, J. A.; Raiziss, G. W., and Weiss, C.: Laboratory and Clinical Studies Bearing on the Causes of the Reactions Following Intravenous Injections of Arsphenamin and Neo-Arsphenamin, Arch. Dermat. & Syph. **1**:235 (March) 1920.

2. Under physiologic limits of H-ion concentration, only traces of inorganic arsenic are bound.

3. Other hydrophilic colloids, such as gum arabic and egg albumin, react in a similar way with arsphenamin and inorganic arsenates.

4. The protection afforded by hydrophilic colloids against the agglutination of red blood cells by arsphenamin is due to the union of the former with the latter, thus preventing the binding of the arsphenamin by the cells. This is the physiologic method of protection which operates after the administration of therapeutic doses.

5. The change in the coagulating properties of the plasma proteins after the injection of arsphenamin may be explained by the assumption that the compound with arsphenamin is soluble at certain H-ion concentrations.

A NOTE ON THE PROPHYLAXIS OF SYPHILIS FROM THE WRITINGS OF DANIEL TURNER, M.D. (HONORARY), YALE, 1723.

J. E. LANE, M.D.
NEW HAVEN, CONN.

The historians of Yale—Dexter and Stokes—in their studies of the lives and achievements of the graduates of their alma mater, have gone over the ground so thoroughtly that one may reasonably have little hope of success in picking up any gleanings left behind them. It was my interest in the early history of syphilis and dermatology which led me by accident to the discovery of the fact, not previously noted, that Yale's first Doctor of Medicine, Daniel Turner, and the notorious dermatologist and syphilographer—the Dirty Old Daniel of Wadd—were one and the same person.[1]

You are familiar with the details of his gift of books and of how, in the words of Jeremiah Dummer, the Yale authorities did themselves "great honour" by conferring the diploma on him, and you may agree with me in thinking that when Turner's bust is placed in Yale's Hall of Fame, the postscript of the letter which accompanied his gift deserves to be placed under it, engraved on a tablet of "eternal bronze" as a sample of unadulterated brass:

> If your worships consider me worthy of the doctoral degree of Yale Academy and have the diploma sent me, I shall receive it not only as a sign of your gratitude, but I shall consider it an honour as much as though it had been conferred by another university, though of greater note.
>
> Farewell most learned sirs and
> may your academy flourish.

As my interest in the early history of syphilis led me to the discovery of the fact just referred to, so more recently, while reading some of the early history of the prophylaxis of syphilis, I again accidentally ran across an accomplishment in that field with which Turner's name is connected, and which gives him another claim to fame.

Some of the early attempts at venereal prophylaxis were curious, but I shall refer to only one. The first mechanical preventive is attributed to the inventive genius of Fallopius, and was published in

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*Read at the meeting of the Beaumont Medical Club, Hartford, Conn., March 10, 1922.

1. Lane, J. E.: Daniel Turner and the First Degree of Doctor of Medicine Conferred in the English Colonies of North America by Yale College in 1723, Ann. Med. History **2**:367, 1920.

his book, "De Morbo Gallico," which was printed in 1564, two years after his death. I will quote part of Chapter 89, as it makes a fitting and interesting introduction to my subject.

It seemeth to me that I have accomplished naught if I tell you not how one who beholds a most beautiful siren and cohabits with her, though she be infected, may be kept safe from the Gallic decay and pox. I have ever been of this opinion that there be a method of prevention, that ulcers arise not from contagion of this sort. But what is that method? I have said that this decay originates from the communication of diseased corpuscles which are drawn through the pores of the glans and produce disease; and therefore it is necessary that at once we purge this disease from the glans; but if it be absorbed through the pores, though we bathe the penis with wine or with water, nevertheless we cannot rub it away; as this happens often in protected and weak glans. How then are we to proceed? I have been of the opinion that we should apply something that hath the power of penetrating the skin and of dissipating matter, or of drawing it out, or of drying it up, and so defeating it by its own nature; therefore I have sought out this cure. But since it behooveth us to well dispose the minds of whores, we may not bring with us from home an ointment: Wherefore I have invented a linen cloth imbued with the cure which can conveniently be carried, since nowadays you wear such ample thigh clothes that you may have with you an entire apothecaries shop. As often therefore as one will cohabit, let him wash (if he can) his privy part or wipe it with a towel; afterward let him take the linen cloth prepared to match the size of his glans; finally when he cohabits let him place it over the glans and let the foreskin come down over it. If he can wet it with spittle or with wine, it is well; however it makes no difference; if you are afraid that the disease may originate in the middle canal, you should have a fold of this linen and place it in the canal. I have tested one thousand, one hundred cases and I swear by immortal God that none of them received infection. It is to be noted however in passing that any form of clean linen cloth has such preservative power as nothing else: (add to this that new soft cotton well beaten, wrapped around the glans well washed, is a marvelous preservative: and when anyone has dashed his timber against the Gallic rocks, let him behold it after removal; he will see that bloody fold infected with a yellow, white or gray color). Therefore let a man ever wrap his glans with a small linen cloth for four or five hours, and this is not distasteful to the women, but nevertheless the method of a prepared cloth is the very best. Its preparation is as follows:

℞

Rad. Gentian. Aristol. long. tenuis, rotundae ā ʒ j
Pulv. Santal. alb. rub. lign. Aloes ā ℈ ij
Pulv. Coral. Rub. Spod. ex Ebore, C.C. C. ā ʒ ss
Fol. Scord. Sonchi Beton. Scabios. Tormentil. ā Mj & ss
Scob. Guaj. ʒ ij
Squame aeris ʒ ij
Praecipit. pp. ʒ iss
Vini Malvatici opt. potentit ℔ iss
Aq. Sonchi aq. Scabiosae ℔ ij
Assumitur Vinum & Aqua, & in his infunditur scobs Guaj.
per 24 H oras.

Dein adduntur reliqua omniz & bulliunt siml ad Consumptionem medietatis, deinde colatur Decoctum, & exprimuntur medicamenta dilligentissime, In hoc Decocto perturbato maceratur per noctem pannus linteus purissimus, deinde siccatur in umbra, & hoc sit tribus vicibus: Ter enim, aceramus, ter etiam siccamus. Postea paramus frusta ad proportionem propriae Glandis, & semper habentur in Marsupiolo, vel in cavo illius partis femoralium, que Brachetta dictitur.

In spite of Fallopius' great reputation, and even in spite of his swearing "by immortal God" that none of the one thousand, one hundred cases in which he tested his appliance received infection, some of his successors in syphilology have been inclined to question his veracity. I feel that we are not radical in assuming that at least he probably did not have one of our modern, efficient follow-up systems at his disposal.

As no more efficient appliance appeared on the scene for a hundred and fifty years, we will skip the intervening period and turn our attention to Turner.

In his book on "Syphilis," published in 1717, the following passage is found. (I quote from the second edition, London, 1724, page 82, as the first edition was not accessible.)

The sin of Whoring (if our very polite Age will allow me the Expression) is become so epidemical and spreading, that to humour the Votaries, who are both more forward and frequent in paying their Devoirs at Venus's Temple, than any other; and consequently under Necessity of an often Penance, which we must needs think very cloying to the other Appetite: We have those who pretend to have found out a Preservative, taken beforehand; but that Fallacy being detected, and carrying too much of Contradiction in the Thing itself, to take Place: (unless with very few of the shorter-sighted) Another soon after, set up for the Cure without any Physick at all, (a special Bait for an old surfeited Sinner) only by the external or local Application: Yet here, if we duly consider the Nature and Subtility of Poisons (and our Disease is no other than the Result of a *Venenum sui generis*) together with that of the animal Compages; which is either tubular or vesicular, permeable as well as perspirable in all its Parts: We shall find but little Safety in relying upon these pretenses. For were the whole Duct of the *Urethra*, an open Canal upon the *Dorsum Penis;* (as it lies incompast and arch'd over, as it were by the nervous Bodies thereof) and that also the undoubted Seat of the first Taint: Nevertheless without the internal Prescription, we should, I fear, be at a loss to secure many of our Patients, by the sole Use either of the best Preventives, Defensative or other topical and chirurgical Applications whatever; we frequently see this, in some simple or slight Frettings on the *Prepuce*, but much more in *Chancres*, where although the Remedy has immediate Access to the Part, and the Ulceration is digested, deterged, and cicatrized by mercurial Applications; (and 'tis rare that any other will avail) yet if the Patient trust only to this Part of Regimen, 'tis odds if some time after he be not forced upon taking much more Medicine, and of undergoing a severer Discipline, than he need have done at first: Not to mention oftentimes the Difficulty, if not the Impossibility of healing some of these Ulcers, without the internal Assistance.

However, if the Method answer (as I believe it neither does nor will) I shall be far from grudging the Gentleman even a Patent (if he can obtain it) for the sole Propriety in this way of Practice.

Whether the *Physician* took the Hint from the *Quack*, or the *Quack* from the *Physician*, is not worth disputing; the *Bait* being like to catch Fools, the *Secret* has since multiply'd: and Dr. *Sharp*, as well as the *Wolverhampton* Surgeon, with two or three others behind the Curtain, stand Candidates with Dr. C——n, for the Glory of the Invention.

As to the *Preservative* in general, I have this only to add farther, that whether any such Thing be possible or not, I shall not take upon me absolutely to determine. But when a certain Gentleman tells us, *That it will become every Man to be modest, when at any time a Method of preventing may be recommended upon due Experience:* I can't further forbear enquiring, whether we may expect the Discovery from a modest Man; or what Reward even a common moral Man will deem him worthy, (without consulting Casuists) that shall first publish it to the World? And indeed when it is revealed, I leave every honest Man to judge of the Consequence; though I think there is no great Danger of such an Invention. The *Condum* being the best, if not the only Preservative our Libertines have found out at present; and yet, by reason of its blunting the Sensation, I have heard some of them acknowledge, that they had often chose to risque a *Clap*, rather than engage *cum Hastis sic clypeatis.*

This passage contains the first known reference to the condom in literature. The book from which it is taken was published a few years before Turner received his Yale degree, and was one of those he sent as a gift to the College. I wonder whether the Reverend Timothy Woodbridge, who conferred the degree, had carefully read the book.

The word is here spelled "condum," and tradition has had it that the article was named after a physician of the same name, or Condom, or Condon or Conton. The medical dictionaries I have consulted, which give the word, say that it is "A corruption of Conton, the name of a physician who first suggested the use of it. He lived in London in the middle of the eighteenth century." This explanation has probably been copied from the Sydenham Society's "Lexicon." It appears that this explanation is a gratuitous assumption for which Swediaur and others were responsible, for careful researches have failed to reveal any physician of this name living in England at about that time. Those who may be interested in the details of the growth of this legend and of the history of the subject are referred to the article by Le Pileur,[2] to which I am indebted for most of the details here given.

My purpose at this time is simply to call attention to another of Turner's almost unknown claims to fame. There are many other entertaining episodes in his medical career and writings. If leisure permits, I may, in the distant future, be able to study him in more detail;

2. Le Pileur, L.: Les Préservatifs de la syphilis à travers les âges, Ann. d. mal. vén., July, 1907, p. 501.

to sketch his progress; to enumerate his disputes with his colleagues and to compare his own estimate of himself with the estimate his contemporaries formed of him.

The story would be interesting and the purpose laudable; for the achievements of Yale's First Doctor of Medicine should not be consigned to oblivion.

INTRAVENOUS INJECTION OF GLUCOSE IN THE TREATMENT OF DERMATOLOGIC CONDITIONS

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Experience teaches us that many skin conditions are cleared up by treatment of a general condition, as they are related to disorders of metabolism. With this in mind, Scholtz and Richter, for the first time, used hypertonic solutions of glucose intravenously in the treatment of dermatologic conditions, basing their method on the theory of osmosis. They first treated exudative conditions. Later, believing that glucose might produce excitation of cellular protoplasm, they extended the treatment to other conditions, such as dry eczema, psoriasis, Dühring's disease, pemphigus, Hebra's disease and several kinds of pruritus. Covisa and Bejarano of Madrid obtained good results in treating mercurial erythrodermia, pemphigus foliaceus, chronic eczema, hemorrhagic purpura and leukemia.

I am convinced that diathetic skin conditions should be treated with drugs causing general changes of metabolism; in other words, general, not local, treatment should be used. As I am in charge of a service of skin diseases and syphilis in which 1,000 patients are treated every month, I had an opportunity to try this method. About seventy injections of a 59 per cent. solution of glucose were given at intervals of three or four days, from 16 to 30 c.c. being used for each injection. This treatment was well tolerated.

I failed to obtain results in the treatment of Hebra's disease, in Wilson's dermatitis exfoliativa, in Dühring's disease, in psoriasis and eczema; but I obtained good results in several kinds of pruritus, including anal and vulvar, which are particularly resistant to other therapeutic measures. I agree with Covisa and Bejarano that glucose causes improvement in edema of the legs due to varices or ulcers.

BROMIN ERUPTION BY PLACENTAL TRANSMISSION

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A bromin rash occurring in the new-born as a result of the administration of large doses of bromids to the mother in late pregnancy is a rare or unique condition. It means that bromin can go through the placenta and have its effect on the unborn child.

In December, I was called to St. Ann's Hospital to see a child born of an eclamptic mother. The child had never been nursed from the breast of the mother, nor had it been given any drugs. Its food consisted of Eagle Brand milk.

The following history was obtained: During the latter part of the mother's pregnancy large doses of bromids had been taken by her, but at no time did she show a bromin rash. The mother's Wassermann reaction was negative. Three days after birth a rash appeared about the eyes of the infant, gradually involving the arms, hands and thighs, with isolated patches on the lower part of the abdomen. A description of the lesion was made by the late Dr. Hardaway as follows: "An acne-like papulopustular and pustular eruption about the arms, legs and lower part of the abdomen. A few of the lesions are discrete, the others confluent. The papular lesions are studded with pustular points. There is a certain resemblance to smallpox, but the character of the lesions taken as a whole and the distribution, together with the history of bromids being given to the mother, makes the diagnosis of bromoderma a most plausible one."

A sample of the patient's urine was obtained and examined by Harry Bristow, professor of chemistry at St. Louis University, who reported that he found a definite trace of bromin in the urine. After two weeks the rash began to disappear and has not recurred. So far as I have been able to review the literature, this is the first case of bromin eruption occurring in an infant as a result of transmission of bromids through the placental circulation.

Abstracts from Current Literature

STUDIES IN FAMILIAL NEUROSYPHILIS. II. FAMILIAL NEUROSYPHILIS FROM VARIOUS EXTRAFAMILIAL SOURCES: A CLINICAL CONTRIBUTION TO THE QUESTION OF NEUROTROPISM. J. E. Moore and A. Keidel, J. A. M. A. **80**:818 (March 24) 1923.

In three families under the author's observation, all members contracted syphilis, and all developed some form of neurosyphilis. Each contracted syphilis from a different source and at widely separated dates. This occurrence can best be explained on the basis of familial predisposition. Clinical and experimental evidence now available does not settle the question as to the existence of a neurotropic strain of *Spirochaeta pallida*.

CLINICAL EXPERIENCE WITH KOLMER COMPLEMENT-FIXATION TEST FOR SYPHILIS. J. F. Schamberg and S. S. Greenbaum, J. A. M. A. **80**:836 (March 24) 1923.

Besides reviewing the published reports on Kolmer's new technic, the authors cite their own experience with it based on more than 4,000 tests in more than 400 cases.

A false positive reaction with the new technic has never been encountered. The authors report a case of leprosy in which the older three antigen tests gave a four plus reaction, the Kolmer test being negative. They also found it more sensitive than the older technics. Its sensitiveness is shown by the longer time required to obtain a negative Wassermann reaction after the institution of treatment, the quicker return from negative to positive following a period of latency, and the earlier appearance of the test in primary cases. The Kolmer test was often positive in tertiary cases when the usual three antigen technics gave negative reactions.

Schamberg and Greenbaum regard the Kolmer test "as an invaluable advance in the serologic study of syphilis."

TRANSFUSION IN PURPURA HEMORRHAGIA. R. C. Larrabee, J. A. M. A. **80**:838 (March 24) 1923.

No matter what the underlying condition, hemorrhagic purpura is always due to a numerical decrease of blood platelets. The life of a blood platelet in the blood stream is only a few days. In view of these facts, it is logical to use frequently repeated transfusions of whole unmodified blood. Three cases are reported in which this treatment was carried out with satisfactory results.

Michael, Houston, Texas.

THE WASSERMANN REACTION WITH LIQUOR FOLLOWED BY EXAMINATION OF THE EXTRACT. Savnik and Kogoj, Arch. f. Dermat. u. Syph. **140**:346, 1922.

Extract doses which are too small compared with serum or liquor doses are likely to furnish incorrect positive results. The liquor Wassermann reaction must be made with negative and positive liquor controls.

Ahlswede, Buffalo.

IRRITATION OF THE SKIN AND ITS USE. HAMMER, Dermat. Wchnschr. **75**:969 and 996 (Sept. 30 and Oct. 7) 1922.

The irritability and susceptibility of the skin to the various types of irritation is considered broadly, and also the effect of continued irritation. The value of irritation, external or internal (the latter chiefly through the use of arsenic) is described, when applied at suitable times in suitable cases.

HYPOSUSCEPTIBILITY OF THE SKIN OF A NEVUS TELANGIECTATICUS AGAINST ACUTE ECZEMA. L. WAELSCH, Dermat. Wchnschr. **75**:982 (Sept. 30) 1922.

In a patient, aged 58 years, an extensive eruption did not involve a large nevus, but stopped short at its borders. By way of investigation the author applied 50 per cent. croton oil in olive oil to the skin of another patient with a similar nevus, the nevus being exempt in the ensuing dermatitis.

ANSWER TO DELBANCO'S OBSERVATIONS ON NOURNEY'S IMMUNITY-TREATMENT OF THE VENEREAL DISEASES. NOURNEY, Dermat. Wchnschr. **75**:985 (Sept. 30) 1922.

In reply to Delbanco's recently published criticism, the author once more argues in favor of his theories as to the efficacy of autogenous serum injections in the treatment of gonorrhea and syphilis.

CONTRIBUTION TO THE QUESTION OF DIFFUSE SKIN INFILTRATION IN THE SECONDARY STAGE OF SYPHILIS. EVENING, Dermat. Wchnschr. **75**:993 (Oct. 7) 1922.

In a woman, aged 44 years, with mucous patches in the mouth and a positive Wassermann reaction, there was a diffuse erythematous circumoral infiltration with rhagades, which responded at once to injections of neo-arsphenamin, scars persisting. This must have been a case of acquired rather than of congenital syphilis, similar to the two reported by Savnik (Arch. f. Dermat., vol. 136), showing that diffuse skin infiltration and rhagades may occur in acquired syphilis as well as in the congenital type.

NECROPSY FINDINGS IN A CLINICALLY CURED CASE OF LEPRA. PAUL UNNA and ALFRED PLAUT, Dermat. Wchnschr. **75**:1013 (Oct. 14) 1922.

A sailor, aged 59 years, had contracted leprosy of the mixed type, probably in 1902 while in the Malay archipelago. He also had syphilis of thirty years' duration. In 1913, the case was diagnosed and treatment started, iodids being employed at first, and subsequently chaulmoogra oil derivatives, mostly parenterally. In 1919, the active manifestations had vanished, and no organisms could be found in the nasal secretions. This apparently cured state persisted until 1921, when the patient became jaundiced and died. At necropsy, the only evidence of leprous infection was seen in the ulnar nerve, in which the bacilli were found. There was optic nerve involvement, also probably leprous. However, from a public health standpoint, the case had been cured, for the contagious foci had been eradicated.

CONTRIBUTION TO THE SUBJECT OF CUTIS VERTICIS GYRATA. HUGO HECHT, Dermat. Wchnschr. **75**:1035 (Oct. 21) 1922.

With the aid of a photograph, the author describes the case of a man, aged 39 years, the left side of whose scalp is involved. Part of the malformation was at the site of an injury sustained twenty-three years previously.

HETEROPLASTIC SYMMETRICAL BONE FORMATION IN THE SUBCUTIS. E. Fraenkel, Dermat. Wchnschr. **75**:1057 (Oct. 28) 1922.

In a woman, aged 62 years, the skin of both legs contained osseous nodules, demonstrated clinically, roentgenologically and microscopically. Speculating as to their origin, the author supposes the cause to have been diminished tissue nutrition brought about by the atheromatous narrowing of blood vessels in this region. A necrosis of subcutaneous fat cells ensued, the necrotic masses becoming calcified.

SYPHILITIC BILIRUBINEMIA AND ITS TREATMENT BY MEANS OF LINSER'S MIXED INJECTIONS. F. W. Kloeppel, Dermat. Wchnschr. **75**:1065 (Oct. 28) 1922.

Citing six of his cases as illustrations, the author reaches the following conclusions: 1. Bilirubinemia appearing in a fresh syphilitic infection or during the first half of the course of treatment is usually syphilitic in origin, especially when the reaction of Van dem Bergh is negative or retarded. 2. In such a case energetic antisyphilitic treatment is indicated. 3. Mixed injections of an arsphenamin and a mercurial product are to be recommended. The author used neosilver arsphenamin or neo-arsphenamin mixed with mercuric chlorid.

THE HISTOGENESIS OF TAR CARCINOMA. R. Bierich, Dermat. Wchnschr. **75**:1081 (Nov. 4) 1922.

Having applied tar to white mice, the author found that on an average hyperkeratosis ensued forty days after the first application, epithelial hypertrophy after eighty days, and epithelioma after 131 days, with slight variation. If the tar applications were discontinued during the stage of epithelial hypertrophy, epithelioma followed at the usual time. During the pre-epitheliomatous stage, the underlying connective tissue cells became swollen, the proportion of elastic tissue increased, and the number of mast cells was augmented. These dermal and epidermal premalignant changes seemed to be due to the action of the tar itself; they may also be produced by other agents, such as arsenic or roentgen rays. When the epithelioma appeared, these changes vanished. When tar and arsenic were both used, the reaction was increased, and the development of epithelioma was delayed until the one hundred and eighty-eighth day, which would seem to indicate that the earlier changes are protective in nature.

GOLDHYDROSOL AND THE COLLOIDAL GOLD REACTION IN THE CEREBROSPINAL FLUID. W. Prosch, Dermat. Wchnschr. **75**:1085 (Nov. 4) 1922.

The various types of reaction are discussed, and the use of a proper gold solution advised, in which the particles are uniformly 25 microns in their linear dimension, with the correct electrolytic content and hydroxyl-ion concentration, in order that false negative results and irregular curves may be avoided.

THE ACTION OF THE GLANDULAR SECRETIONS OF THE PUBIC LOUSE ON HUMAN BLOOD CELLS IN REGARD TO THE ORIGIN OF MACULAE CERULEAE. F. Grusz, Dermat. Wchnschr. **75**:1105 (Nov. 11) 1922.

The author separated the heads from the bodies of the lice, ground them with quartz and mixed them with physiologic saline or other agents. He

found that the fresh extract was hemolytic, while the extract made from the enteric glands was coagulant to human blood. The various theories of the formation of maculae ceruleae are reviewed. Hematoidin rather than pigment deposits is held to be causative, for the maculae disappear within two weeks, which would be impossible in the case of true pigment.

IS GUIDO BACCELLI THE CREATOR OF INTRAVENOUS THERAPY, ESPECIALLY IN THE CASE OF SYPHILIS? W. SCHONFELD, Dermat. Wchnschr. **75**:1110 (Nov. 11) 1922.

It is often said that Baccelli, in 1893, or Landerer, in 1882, was the first to employ intravenous therapy, but the author finds that it had been used previously both on the European continent and in England. There is a record of its use, probably by Fabritius, in 1665, in the treatment of syphilis, good results having been reported as following the injection of guaiac mixtures containing scammonium.

CONTRIBUTIONS REGARDING THE CLINICAL ASPECT AND DIAGNOSIS OF THRUSH INFECTIONS OF THE SKIN. A. ALEXANDER, Dermat. Wchnschr. **75**:1125 (Nov. 18) 1922.

The author reports four cases of this infection, all in women between 40 and 75 years of age, the first being a diabetic patient with plaques in the genitocrural region resembling those due to trichophytosis, and in addition scattered pustules on the thighs; in the second patient the lesions were about the toes, in the third, there were genitocrural plaques and in the fourth, both the genitocrural and mammary regions were involved. As diagnostic criteria, the author calls attention to the clinical picture, presenting diffusely scattered or closely grouped, often ring-shaped pustular efflorescences, resembling intertrigo; the typical clusters (not chains) of spores among the mycelia, found after potassium hydroxid has been added to the scales; the cultural characteristics on beer wort agar and on Sabouraud's mediums, fully developed within ten days.

A CASE OF NEVIFORM ANGIOKERATOMA. H. BOCKHOLT, Dermat. Wchnschr. **75**:1132 (Nov. 18) 1922.

A single small tumor, apparently present since birth or very early childhood on the penis of a patient, aged 22 years, was excised and showed the histologic characteristics of the angiokeratoma of Mibelli. The author considers it a true nevus.

THE HEMOLYTIC COMPLEMENT OF BLOOD, ESPECIALLY IN SYPHILIS. B. VON LANDMANN, Dermat. Wchnschr. **75**:1134 (Nov. 18) 1922.

The author has found that in early syphilis there is a rather infrequent slight diminution of complement; in paralysis the diminution is commoner and more appreciable. The disappearance of complement occurs mostly in vitro, but at times it is detectable very soon after the blood has been taken. The protecting action of the blood clot when the serum is heated to 37 C. is due to materials present for the most part in the blood corpuscles, but also in the plasma. In the destruction of complement the intermediate stage is more active than the end stage, as is demonstrable by a twenty-four-hour incubation of the serum at 37 C., followed by a half hour's inactivation at 56 C.

CONTRIBUTION TO THE CASUISTICS OF MYCOSIS FUNGOIDES. E. WELLMANN, Dermat. Wchnschr. **75**:1149 (Nov. 25) 1922.

A man, aged 48 years, who had had the disease for at least one year, presented many tumors, none of which were ulcerated, and there was a generalized lymph node enlargement. The histologic picture at first suggested that of lymphosarcoma, but was really typical of mycosis fungoides. Through a filter of 2 mm. of aluminum a full erythema dose of roentgen rays was given to the nodules, and the affected skin elsewhere received one-half of an unfiltered erythema dose. Six weeks after the institution of this treatment nearly all of the tumors had vanished, and there was no more itching; the lymph nodes were still enlarged.

STATISTICS CONCERNING VENEREAL DISEASES IN MARRIED PERSONS. L. VOIGT, Dermat. Wchnschr. **75**:1153 (Nov. 25) 1922.

At the author's clinic the percentage of syphilis in married men is about 23, in married women, about 22. Other statistics are given, and the need of careful treatment and family observation is urged.

INFLAMMATORY CYSTIC CHANGES IN THE SWEAT DUCT ORIFICES IN A SCARLATINIFORM ERUPTION. A. M. SCHOCH, Dermat. Wchnschr. **75**:1169 (Dec. 2) 1922.

In a youth dying with acute polyarthritis and endocarditis, on the final day there had appeared a generalized scarlatiniform eruption with small vesicles scattered here and there. Microscopic search revealed degenerative changes in the epidermal cells adjoining the sweat ducts, with cyst formation and signs of slight inflammation. There was no visible change in the sweat glands themselves. In the basal cells of the epidermis there were peculiar changes in the cytoplasm, not resembling those seen in scarlatina. Three excellent colored plates illustrate the microscopic findings.

PURPURA HEMORRHAGICA WITH HEMATURIA AND FATAL PULMONARY HEMORRHAGE AFTER THE ADMINISTRATION OF NEO-ARSPHENAMIN. F. CALLOMON, Dermat. Wchnschr. **75**:1197 (Dec. 9) 1922.

An apparently robust man, aged 25 years, with no history of hemorrhagic manifestations, was given 0.15 gm. of neo-arsphenamin, and after a week, 0.3 gm., two injections of mercury salicylate having also been given. Immediately after the second arsenical injection, small hemorrhagic punctae appeared, and within a few days death ensued. At necropsy, hemorrhagic areas were found in all parts of the body except the intestines. The number of blood platelets was distinctly increased.

A CONTRIBUTION TO THE QUESTION: LICHEN PLANUS OR ARSPHENAMIN ERUPTION? W. MARENBACH, Dermat. Wchnschr. **75**:1233 (Dec. 23) 1922.

The author reviews the literature and describes a case in which the administration of silver arsphenamin was followed by the appearance of an eruption almost similar to lichen planus, with the linear and garland-like arrangements of the papules and suspicious lesions in the mouth. However, in the opinion

of the author, the color of the lesions was too brightly erythematous, and the duration of the outbreak too short to warrant a diagnosis of true lichen planus. Ther was no biopsy examination.

METABOLISM AND SKIN DISEASES. I. CHOLESTERIN. E. PULAY, Dermat. Wchnschr. **75**:1236 (Dec. 23) 1922.

The author found a hypercholesterinemia in seborrhea, urticaria, pruritus, eczema, prurigo, psoriasis, rosacea, erythema nodosum, xanthoma, lupus erythematosus and other skin conditions, but the significance of its presence is not clear. Its function may be that of a protector.

CONTRIBUTION TO OUR KNOWLEDGE OF MORPHEA GUTTATA. E. PICK, Dermat. Wchnschr. **75**:1253 (Dec. 30) 1922.

A woman, aged 46 years, had grouped lesions on the abdomen, buttocks and thighs, of a few months' duration. Histologic study showed the presence of collagenous hypertrophy. The author classifies the condition as a true scleroderma.

THE CURE OF STAPHYLOGENIC SYCOSIS BY CATAPHORESIS. F. WIRZ, Dermat. Wchnschr. **76**:3 (Jan. 6) 1923.

In nine out of ten cases of stubborn sycosis of years' duration, the author, by means of cataphoresis, was able to bring about a cure in from four to twelve weeks. At first, in each case, a 10 to 20 per cent. aqueous solution of ichthyol was used, with exposures of ten to fifteen minutes' duration about every second day, the current strength being 5 to 10, or even as high as 20 milliamperes. When the outbreak had been soothed somewhat by this means, diluted Lugol's or Gram's solution was substituted, with a current strength of about 5 milliamperes and exposures lasting from three to five minutes, until a cure was brought about.

THE TREATMENT OF PEMPHIGUS. J. ISER, Dermat. Wchnschr. **76**:8 (Jan. 6) 1923.

The author describes the course of pemphigus foliaceus as it occurred in a young Jewish medical student, with a fatal termination within two months in spite of attempts at treatment. He also recounts the case of an old man whose pemphigus vegetans was apparently cured by small doses of neo-arsphenamin, later reinforced by quinin and trypaflavin. For the treatment of pemphigus vulgaris, the arsphenamins, quinin, serum and trypaflavin are recommended.

THE INTRAVENOUS ADMINISTRATION OF THE ARSENICALS AND SIMILARLY ACTING DRUGS WITH REGARD TO THEIR PHARMACODYNAMIC ACTION ON THE LIVER AND OTHER ORGANS. K. ULLMANN, Dermat. Wchnschr. **76**:29 (Jan. 13) 1923.

The author illustrates his brief review of the subject with six excellent photomicrographic plates showing the fatty changes in the liver and kidney following the administration of large doses of potassium arsenite solution (Fowler's solution) and neo-arsphenamin to dogs and rabbits.

BRUCK'S REACTION, A NEW PRECIPITATION TEST FOR THE SEROLOGIC DIAGNOSIS OF SYPHILIS. G. JAHNKE, Dermat. Wchnschr. **76**:33 (Jan. 13) 1923.

In over 500 cases the author compared this new method with those of Wassermann, Sachs-Georgi and Meinicke, finding it very valuable, giving non-syphilitic results only rarely, and being quickly carried out.

NOURNEY'S IMMUNITY TREATMENT OF THE VENEREAL DISEASES. EVENING, Dermat. Wchnschr. **76**:36 (Jan. 13) 1923.

At the clinic in Dusseldorf, this method has been thoroughly tried and found apparently worthless.

THE TREATMENT OF LUPUS VULGARIS OF THE NASAL MUCOSA. ESCHWEILER, Dermat. Wchnschr. **76**:38 (Jan. 13) 1923.

The author recommends the use of the ultraviolet light with an intranasal applicator.

THE EVALUATION OF FINDINGS IN THE CEREBROSPINAL FLUID IN INCIPIENT, EXANTHEMATIC, LOCALLY RECURRING AND EARLY LATENT SYHILIS. J. LEYBERG, Dermat. Wchnschr. **76**:53 and 86 (Jan. 20 and 27) 1923.

In incipient syphilis, before the appearance of the eruption, the author has found the occurrence of hematogenous infection of the central nervous system in 7.8 per cent. of cases, a pleocytosis being the most common sign, a positive globulin reaction occurring only one-fourth as frequently, and a positive Wassermann reaction never occurring in the fluid. During the exanthematic stage of the disease, one third of the cases showed changes in the spinal fluid, pleocytosis being the most frequent finding, and its occurrence in proportion to that of globulin and a positive Wassermann reaction in the fluid being as 37 : 12 ; 5 : 14. A papular eruption is much more likely to be accompanied by spinal fluid changes than is a macular eruption, in the ratio of 17 to 7. In the stage of early recurrences, pleocytosis, globulin and a positive Wassermann reaction were observed commonly and with about equal frequency, a pathologic fluid being especially likely to be found in cases of syphilitic alopecia and leukoderma. In the early latent cases, pathologic changes in the fluid are seen less often, pleocytosis being infrequent, while a positive Wassermann reaction occurs more often ; the globulin reaction accompanies organic nerve disturbances.

METABOLISM AND SKIN DISEASES. II. CALCIUM. E. PULAY, Dermat. Wchnschr. **76**:81 (Jan. 27) 1923.

In various dermatoses, including the commoner ones, the calcium-ion concentration and the calcium content of the blood were estimated, and found to vary somewhat from what had been expected. This would perhaps indicate that the colloidal side of the question is of great importance, and that much may depend on the calcium content of the tissues.

THE TREATMENT OF SYPHILIS WITH BISMUTH. J. GUSZMAN and M. POGANY, Dermat. Wchnschr. **76**:125 (Feb. 10) 1923.

Using a 10 per cent. suspension of the bismuth salts in olive oil, the author treated twenty-one patients, most of whom presented active secondary lesions ; and the results were encouraging. He states that the drug may be used simul-

taneously with the arsenicals and mercurials, but he has seen no great benefit arise from this combined therapy. It now seems that this new medication may be ranked with mercury and close to arsenic.

CUTANEOUS IRRITATION AFTER THE APPLICATION OF MOIST CELLULAR DRESSINGS. E. SCHAUKE, Dermat. Wchnschr. **76**:137 (Feb. 10) 1923.

Sulphuric acid derivatives incorporated during the manufacture of the dressings seemed causative, so that they can no longer be used except with extreme care.

EXPERIENCES WITH LINSER'S MIXED ARSPHENAMIN-MERCURY TREATMENT. O. EBEL, Dermat. Wchnschr. **76**:105, 133 and 158 (Feb. 3, 10 and 17) 1923.

If the dosage be sufficient and the interval between courses not too great, the author considers this form of treatment the most effective. His minimum dose of neo-arsphenamin for women is 0.45 gm., with 0.02 gm. of mercuric chlorid, a total of 4 to 5 gm. of the arsenical drug being the minimum requirement for the completion of the first course. After a vacation which must not exceed eight to twelve weeks, a second course totaling 3 gm. is given. Injections may be given once or twice a week with apparent safety.

HYPERKERATOTIC ERUPTIONS ACCOMPANYING GONORRHEA AND THEIR RELATIONSHIP TO PSORIASIS. BUSCHKE and LANGER, Dermat. Wchnschr. **76**:145 (Feb. 17) 1923.

An old gonorrheal infection in a young woman was accompanied by a polyarthritis and a hyperkeratotic and pustulocrustaceous eruption of the axillae, chest, feet, umbilical and genital regions. Sections showed no organisms. This condition is rare in women. Discussing its etiology, the authors say that the skin may be congenitally predisposed to eruptions of this type.

PARKHURST, Toledo, Ohio.

ECZEMA SEBORRHOICUM AND PSORIASIS. SIEBEN, Deutsch. med. Wchnschr. **48**:357, 1922.

The author discusses Riecke and Unna's conception of the etiology of psoriasis. He describes two cases which support Unna's theory that psoriasis and seborrhea are two branches of the same diseased trunk. A female patient with pronounced seborrhoic eczema of the scalp developed, during the course of treatment, several isolated typical patches of psoriasis.

TREATMENT OF HYPERHIDROSIS. JOSEPH, Deutsch. med. Wchnschr. **48**:557, 1922.

In mild cases, painting with a 1 or 5 per cent. solution of chromic acid is advised, also overnight application of salicylic powder. In obstinate cases, large doses of hard roentgen rays are recommended.

ARSPHENAMIN IN THE SURGERY OF SEPTIC WOUNDS. GEYER, Deutsch. med. Wchnschr. **48**:806, 1922.

The author describes a new disease picture under the name of edema cutis proprium. He develops a new theory of the pathogenesis of edema, basing his deductions on the therapeutic results obtained in a case in which he elim-

inated every trace of sodium chlorid from the food of the patient. Pathologic tissue alterations of the skin disturb the metabolism of the cutis cells, thereby causing retention of colloids and the accumulation of sodium chlorid, which causes increased retention of water.

NERVE PARALYSIS AND NERVE STIMULATION WITH REGARD TO THE DEVELOPMENT OF TROPHIC TISSUE ALTERATIONS.

Bruening, Klin. Wchnschr. **1**:729, 1922.

In the pathogenesis of vasomotor and trophic disturbances, a stimulation of the nerve is generally the causative factor, seldom a paralysis of the nerve. This is proved by many trophic disturbances which were caused by neuromas and which disappeared on surgical removal of the neuroma. A pathologic stimulation increases the tonus in the sympathetic region. In a case of vasomotor—trophic neurosis, the author effected complete cure by periarterial sympathectomy.

METHOD FOR OBTAINING THE "WASSERMANN SUBSTANCE."

Citron, Klin. Wchnschr. **1**:1102, 1922.

The antigen-syphilis serum is prepared first. The deposit is dissolved in 1.7 per cent. sodium chlorid. The solution is then placed on a suitable colloid filter, through which only the "Wassermann substance" passes. This substance, obtained by filtration, can at any time be bound by antigen whereby complement is permanently used up. The substance therefore has all the qualities of a genuine amboceptor, in the sense of Ehrlich. The choice of the correct filter caused considerable difficulty and retarded an earlier publication of this process by Wassermann.

PHYSIOLOGIC EFFECT OF LIGHT ON THE ORGANISM.

Hansen, Klin. Wchnschr. **1**:1469, 1922.

While ultraviolet rays have a direct chemical effect in the superficial skin layers only and only influence the system indirectly, the visible rays penetrate the skin, are absorbed by the blood and are thus beneficial to the entire system. The best light sources are those in which the composition is nearest that of the sun's rays; that is, the electric arc light.

MULTIPLE TUBERCULOUS ABSCESSES OF THE SUBCUTANEOUS TISSUE CONCOMITANT WITH TUBERCULOUS ARTHRITIS.

Gorke, Med. Klin. **18**:499, 1922.

In a man, aged 47, the author found the rare coincidence of multiple pustular tuberculous lesions in the skin with tuberculous arthritis. Acid-fast bacilli were found in the blood and tubercle bacilli in the pus. As a mixed infection with ordinary cocci was excluded, this case proves that the tubercle bacillus can cause genuine pustular inflammations. The macroscopic and microscopic picture of the skin differed entirely from that of the cold abscess. The polymorphonuclear leukocytes were increased to 75 per cent.

THE IRRITATING EFFECT OF SOAPS ON THE SKIN AND HOW TO COMBAT IT.

Siebert, Med. Klin. **18**:1059, 1922.

It is not only the liberated alkali which causes irritation, but the soap as such has a certain cell damaging influence, as the author proved by hemolytic experiments. He recommends the use of "over-fatted" soaps.

OBSERVATIONS ON ARTIFICIAL LIGHT EFFECT ON THE SKIN CAPILLARIES. THEIR EVALUATION AS A BIOLOGIC MEASURE FOR DOSAGE IN DEEP ROENTGEN-RAY THERAPY. WELCH, München. med. Wchnschr. **69**:546, 1922.

In order to ascertain previous to irradiation a possible hypersensitiveness to roentgen rays as found in some patients, the author advises a trial exposure to quartz light for two minutes at a distance of 50 cm. on a surface of 5 by 2 cm. in the infraclavicular region. Six hours later, the erythema which is provoked is examined with the capillary microscope. The "normal" skin would then show slightly dilated vessels, a slight increase of the blood-current and increased blood contents of the capillaries. These symptoms are most pronounced in nephritis, syringomyelia, diabetes, urticaria, exophthalmic goiter, and Raynaud's disease. Trial irradiation is indicated wherever hypersensitiveness to the roentgen rays could be expected.

CONTRIBUTION TO THE SERODIAGNOSIS OF SYPHILIS BY A NEW METHOD. BRUCK, München med. Wchnschr. **69**:569, 1922.

To 0.2 c.c. of inactivated serum (56 degrees in thirty minutes) in a test tube, the author adds 0.8 c.c. of a salt solution and 0.2 c.c. of a well shaken extract suspension. The tube is then shaken and immediately centrifuged for twenty minutes. The mixture then appears clear with a thin film on the surface. Careful shaking (in positive syphilitic serums) then causes this film to form a characteristic, macroscopically visible flocculation, while negative serums do not flocculate but turn homogenously turbid. The advantages of this method are: 1. The incubator and agglutinoscope are not necessary. 2. The result can be read within thirty minutes. 3. It is clinically equivalent if not superior to the Wassermann reaction. 4. The turbid extract allows the use of the same constant dilution of extract.

STAINING EXPERIMENTS ON SYPHILIS SPIROCHETES WITH NEO-ARSPHENAMIN. KRANTZ, München. med. Wchnschr. **69**:586, 1922.

Preliminary treatment with acetic acid and liquor formaldehydi followed by staining with a 1:1,000 solution of neo-arsphenamin and after treatment with a 1 per cent. ammoniated silver nitrate solution gives an excellent picture of *Spirochæta pallida*. The method is superior to Fontanas', as the pallida is not swollen and appears thin and normally delicate.

PRELIMINARY ADMINISTRATION OF CAFFEIN IN THE ARSPHENAMIN TREATMENT OF THE CENTRAL NERVOUS SYSTEM. SACK, München. méd. Wchnschr. **69**:889, 1922.

In caffein the author believes that he has found an agent which enables us to force more arsphenamin into the spinal canal than ordinarily enters it. Caffein causes an elective constriction of the mesenteric vessels, thereby altering the distribution of the blood in the system and leading more blood to the skin vessels and the central nervous system. Sack holds that the large quantities of arsphenamin which shortly after injection are found in the liver, kidneys and intestines have practically no effect on the spinal cord and the meninges. If caffein can block the blood supply to these organs, arsphenamin can have its effect at other places. Sack injects 0.2 gm. caffein subcutaneously ten minutes before each arsphenamin injection. A report on the practical results cannot yet be given.

ROENTGEN-RAY ERYTHEMAS OF THE ABDOMEN EXAMINED WITH THE CAPILLARY MICROSCOPE. SCHUGT, München. med. Wchnschr. **69**:1178, 1922.

The author examined ninety-eight cases of erythema of the abdominal skin, using a magnification of 103. The results obtained show that in a large number of cases a skin erythema dose weakens the vasoconstrictors, while some vessels appear to be destroyed entirely. After three skin erythema doses, the vessels on the same skin surface are considerably diminished in number. The walls of the capillary vessels also lose their elasticity. The blood current did not appear to be influenced. Hence the histologic alterations cannot be due to a disturbance of the circulation.

CHRONIC UNIVERSAL ARGYRIA AFTER INTRAVENOUS AND ORAL ADMINISTRATION OF COLLARGOL. TOBLER, Schweiz. med. Wchnschr. **52**:774, 1922.

The author reports a case in which the bulk of the silver was found in the glomerules of the kidney and the hepatic arteries. He believes that silver arsphenamin by accumulation could also cause a universal argyria.

INFLUENCE OF VARIOUS KINDS OF LIGHT ON BLOOD PRESSURE. KIMMERLE, Strahlentherapie **13**:299, 1922.

Irradiation with the electric arc light causes a more rapid decrease of the blood pressure than can be obtained by the ultraviolet rays.

GENERAL INDICATIONS FOR ROENTGEN-RAY TREATMENT OF MALIGN TUMORS. SCHMIEDEN, Strahlentherapie **13**:431, 1922.

If possible, carcinoma should be operated on and prophylactic irradiation should follow. The employment of energetic irradiation once before every operation is gaining in importance. Carcinoma of the face should, for cosmetic reasons, be treated by irradiation. Sarcoma should, as a rule, receive the same treatment.

THE EFFECT OF EPINEPHRIN ON THE GLANDS OF TOAD SKIN. WASTL, Ztschr. f. Biol. **74**:77, 1922.

Epinephrin increases the secretion of the glands of the skin.

CULTIVATION OF THE TUBERCLE BACILLI IN LIQUID MEDIUMS WHICH CONTAIN YOLKS OF EGGS. BOECKER, Ztschr. f. Hyg. u. Infektionskrankh. **95**:344, 1922.

The author used a new medium for cultivating tubercle bacilli to great advantage. It consists of a 5 per cent. suspension of yolk of egg in distilled water, to which an alkali is added until the solution clears up.

AHLSWEDE, Buffalo.

Society Transactions

CHICAGO DERMATOLOGICAL SOCIETY

Annual Meeting, Jan. 17, 1923

HAROLD N. COLE, M.D., *Presiding*

ARSPHENAMIN DERMATOSIS TREATED WITH SODIUM THIOSULPHATE. Presented by DR. MITCHELL.

A Chinaman, aged 25 years, who received his first injection of arsphenamin on Jan. 4, 1923, developed a bright red papular eruption the day following the third injection of 0.4 gm. He had been treated with daily intravenous injections of sodium thiosulphate since January 10, with complete healing.

DISCUSSION

DR. PUSEY asked whether the result of treatment in this case was as brilliant as one had been led to expect that it would be.

DR. MITCHELL said that he had had an opportunity to study only a few of these cases. He had only had three cases in the syphilis clinic. The patient presented was first treated with intravenous injections of sodium thiosulphate on January 10, and at that time the eruption appeared red and had the characteristics which would lead him to believe that it was an arsphenamin dermatosis. It might have been a toxic eruption due to something else, but apparently it was an arsphenamin process. With the beginning of treatment the eruption promptly subsided, and it was apparently a brilliant result of the treatment advocated by McBride and Dennie of Kansas City.

DR. SWEITZER said he had three cases, two in women and one in a man. They were all severe, particularly the one in the man, the skin being involved from head to foot with lesions probably ¼ inch (6.35 mm.) thick all over. He was irrational for a number of days, but the skin was now normal, although he had expected the patient to die. The result of treatment was satisfactory. Whether the improvement was due entirely to treatment or whether these patients would have recovered without it, was a question. The treatment was probably a factor, and he thought the sooner it was instituted the better.

DR. RAVITCH asked whether it would not be a good plan to give injections of sodium thiosulphate before giving the arsphenamin.

DR. CONRAD said he had had only one case in St. Louis in which he gave the sodium thiosulphate with good results. They did not seem to get as many of these cases as he had read of in other parts of the country. On an average, they probably gave from seventy-five to a hundred doses each week in the clinic, and they had had only this one case during the last five years. The result of treatment was remarkable. He thought the earlier the cases were seen, the better would be the results.

DR. STOKES said if any results were to be expected, one should give frequent large doses of the thiosulphate; 0.45 gm. every three or four days would not be very effective. The administration of 0.75 or 1 gm. every day would be more likely to produce results. They had had one case which promised to

be severe since Dr. Dennie presented his paper, and the patient would probably have died if she had not been given the drug. The exfoliation was milder, and the course was less severe.

Dr. Stokes said he believed the medical profession should be warned about conclusions on these cases. Many of them clear up irrespective of what is done, and sometimes irrespective of what is done they continue in an unfavorable course. He believed this method was undoubtedly an aid in the treatment of these cases, but thought there was a reason for not giving the drug as a prophylactic as the sulphur would neutralize both the toxic and the therapeutic effect. If given in connection with arsphenamin, it would diminish the efficiency of that therapy.

Dr. Grindon agreed with Dr. Stokes that one should not be in too much of a hurry to argue from good results, and related two cases in point. A man in early life had had a sore but had had no symptoms since. He secured a Wassermann test and at the same time had his wife's blood tested. She had never had a symptom of any kind, but while the husband's blood was negative, his wife's gave a four plus reaction. A physician in another city gave her a series of weekly arsphenamin injections. After the eleventh dose she developed a skin condition. When Dr. Grindon first saw her the condition was extreme. The entire body was covered with bullae and scales, except the tip of each elbow and the palms. She had an acute nephritis with all the symptoms that go with it. He prescribed diluents, a nonprotein diet and consolation, and expected her to die. About three months later she walked into his office perfectly well.

He recently was called to see a case in consultation. The patient had received three doses of arsphenamin within a week. He did not know the dosage. She developed an exfoliative dermatitis and seemed at first to be quite ill. He was considerably alarmed about the case but under purely symptomatic treatment she made a good recovery.

Dr. Grindon believed that while unquestionably Dennie's treatment was well worthy of examination, one should not jump at conclusions. He asked whether any one knew anything about McDonagh's intramin.

Dr. Cole said that in Cleveland they had seen several of the cases of post-arsphenamin dermatitis and had obtained good results with Dennie's treatment. He believed that when one saw a patient show such marked improvement immediately after the drug was used, one must conclude that it had some definite value. One patient came in two months after the characteristic exfoliative dermatitis had started. She was given 40 c.c. of the 1 per cent. solution of sodium thiosulphate, and within twenty-four hours was so much improved that she presented an entirely different picture.

Dr. Pusey said he was very much in doubt as to whether the chemical explanation of the treatment was correct. He thought the general view was that this was a real addition to therapy. He knew some conditions disappeared of themselves, but his experience with arsphenamin dermatoses was that they were very difficult to treat and that they did not usually get well. The results reported from the Dennie treatment seemed to him to be exceedingly interesting, and he believed the remedy was worthy of thorough trial.

Dr. Senear said he had talked with Dr. Lespinasse about the Dennie treatment, and he told him that some years ago a genito-urinary specialist in Cincinnati spoke of treating tabes with a dose of mercury which would ordinarily be fatal, following it with sodium thiosulphate, and the patients tolerated the mercury well.

Incidentally, Dr. Senear had treated one patient whom he saw six weeks after the dermatitis began, and within six days the skin was practically clear. Unfortunately, the patient had had pneumonia previously, and died a day or two later from a respiratory infection.

Dr. Mitchell said he had been interested in the possibility of continuing treatment in patients who were susceptible to arsphenamin. A patient was referred to Dr. Ormsby some time ago because of this susceptibility. This patient was a thin woman with tabes. They had attempted to give arsphenamin and to protect the skin by giving injections of sodium thiosulphate, but they were not successful in that the eruption appeared despite the injections. They were now experimenting with the Chinaman, intending to demonstrate whether or not he was susceptible. They intended to give a minute injection without thiosulphate protection, and if he showed no symptoms, they would decide that it was not an arsphenamin dermatosis. If he showed symptoms, they would resume the sodium thiosulphate. Dr. Mitchell said he believed this was an important point to work out. If these patients were susceptible, they would probably always be so, but if they could be protected by this means, the treatment could be continued. Otherwise it would have to be stopped.

PITYRIASIS RUBRA PILARIS. Presented by Dr. Beeson.

A man, aged 37 years, was beginning to show improvement under thyroid medication. The trouble began three years before with reddening and thickening of the palms. The characteristic horny papules appeared soon thereafter on the backs of the fingers and hands. Later, the soles also showed thickening and fissuring. The trunk, scalp and face have always been free. At the time of presentation, pathognomonic lesions were present on the backs of the fingers and wrists, while the nails showed a decided thickening. Blood chemistry findings were negative.

A CASE FOR DIAGNOSIS. Presented by Drs. Pusey and Senear.

A man, aged 26 years, had a disorder which had been present for about a year, when he first noticed a dark patch in the right malar region. That patch had enlarged, while others had appeared below it, and smaller patches had developed on the opposite side of the face. There was slight itching and tingling when the lesions were covered with perspiration. The patient said that he never took laxatives and that no cosmetics had been used except bay rum and cold cream. The tonsils and teeth had been treated once or twice with silver nitrate, but not until after the pigmentation had begun.

At the time of presentation, there were a number of irregularly outlined slate-colored patches which involved the bearded region on each side of the face.

DISCUSSION

Dr. Senear said the patient stated when he came in that he had never taken any laxatives, but today some one had called his attention to the fact that the man said he had been taking phenolax wafers; and the patient admitted that he took them occasionally.

Dr. Ravitch said he believed the condition did not look like a phenolphthalein eruption, but that it resembled an argyria. He believed the man might have received injections of argyrol for a urethritis or possibly for some eye trouble.

DR. PUSEY said he did not believe the fact that it had been discovered that the patient had taken a few doses of phenolphthalein made much difference. The man had patches of gray infiltration down in the skin. They might be due to phenolphthalein, but he did not know of any such phenolphthalein eruption. The lesions were about the color of argyria, but that does not occur in small, circumscribed patches, unless it is caused by the injection of silver. The man would undoubtedly have known if silver had been injected into the jaws. He had thought of Goeckerman's cosmetic pigmentation, but it did not seem to be that condition either. He asked for suggestions because the case was, in his experience, unique. It was similar to a case seen by him and Dr. Ormsby a few years ago, which had ended in death from malignant disease.

DR. SWEITZER said that Dr. Michelson had recently presented a case of phenolphthalein eruption before the Minnesota Dermatological Society, and the appearance of that patient was just like that of the man under discussion. He thought it would be interesting to give this man some doses of phenolphthalein to ascertain whether it would cause some more lesions.

DR. GOECKERMAN said the eruption did not impress him as the type of dermatitis he had seen caused by the use of cosmetics. He had seen three or four other cases since he had reported the first ones, and in all of them they had found mercury in the cosmetic used. They now had six cases, but this one did not impress him as being like any of theirs.

DR. SENEAR said there was a definite lichenification and definite scaling, and these had been present before any treatment was used. They had observed the patient for several months, and there had never been any change. The man was intelligent, and there was no history of any preceding erythema. Neither did the pigmentation correspond with this. Silver nitrate had been used in the treatment of the patient's teeth, but Dr. Senear thought the condition was not argyria, nor did he believe it to be a phenolphthalein eruption.

DR. ORMSBY said that about a year ago a patient from Michigan was presented before the Society. The pigmentation in that case was of about the same shade as that in the patient shown, but was much more extensive. A biopsy was made and the pigment found to be in the corium. There was no sign of other trouble at that time. Acanthosis nigricans was discussed, but there was no sign of this other than pigmentation. That patient gave a history of having taken sodium bicarbonate in large doses for three years in the treatment of a gastric ulcer. Within the past three months, this patient had died of an internal malignant growth. Dr. Ormsby thought the condition was probably a peculiar pigmentation which was induced by an internal malignant disorder.

MACULO-ANESTHETIC LEPROSY. Presented by DRS. EISENSTAEDT and ZEISLER.

A Chinaman, aged 38 years, from the South Sea Islands, who had been in Chicago one year, had a lesion confined to the right forearm, which was said to be of five months' duration. It was a papular eruption spreading peripherally, with an ulcerating border. The ulnar nerve was thickened, and there was anesthesia in the area supplied by it, with atrophy of the interossei.

The patient complained of shooting pains in the arm. Examination revealed no lepra bacillus from the nose; the biopsy was negative for lepra bacilli, and

the Wassermann reaction was also negative. A blood count showed 80 per cent. polymorphonuclears and 4 per cent. small mononuclears.

Treatment had consisted of chaulmoogra oil with ammoniated mercury, 5 per cent., on the arms.

DISCUSSION

DR. STILLIANS said they never had been able to find the bacillus in this case, but the condition cleared up on antileprosy treatment.

DR. PUSEY said he was willing to admit that it was probably leprosy, but he wanted them to find the bacillus. They had found the Chinaman, and that was the first step toward the diagnosis of leprosy when there was something on the skin. He did not wish to accept the diagnosis of leprosy unless the bacillus was found. Without seeing the organism, he believed that this was an unusual case of leprosy.

DR. CRUTCHFIELD said they had twenty-five to thirty cases of leprosy under treatment all the time, and their trouble was not to find the organism. They give the patients ethyl-esters and chaulmoogra oil for several months and then try not to find the bacilli. He thought it very unusual not to find the organism in cases of true leprosy, either in the nasal secretion or the biopsy.

DR. MENAGE said that he often saw cases with typical lesions in which it was not possible to find the organism, and at the State Home such cases had been accepted on their merits as clinical cases of leprosy without the organism being demonstrable. The older the lesions become, after a variable period of maturity, in some cases (the macular type particularly), the more difficult is it to find the organism. He had at present a case of this nature. Dr. Ormsby saw this patient with him last year, a perfectly typical case of the disease, but at no time could organisms be found. The patient had a typical macular anesthetic patch on her arm; the absence of the organism under those circumstances, in the South did not make them hesitate to accept the diagnosis as correct.

DR. LAIN said he had had under observation for two years two cases of leprosy in the same family. All of the secretions showed the organism in one case. The other, a sister of the boy, had the anesthetic type, as typically as the case presented at the meeting, but they could not find the organism in this case. Both of the patients improved under chaulmoogra oil treatment.

EROSIO INTERDIGITALIS BLASTOMYCETICA. Presented by DR. MITCHELL.

A woman, aged 60 years, who was first seen Sept. 22, 1922, at which time the lesions had been present on the webs of the fingers of the left hand for two months, was treated with 2 per cent. copper sulphate solution and four exposures of ½ unit of roentgen rays.

At the time of presentation, the lesions were completely healed.

DISCUSSION

DR. MITCHELL said that in discussing this type of case he repeatedly had emphasized the fact that the disorder resisted therapy. The first patient he saw he had had under observation for a long time. That patient was an obese Jewess who was given aid by several charitable organizations, who had had much matrimonial trouble and therefore perhaps did not carry out the treatment thoroughly. There was evidence that she had used Whitfield's oint-

ment or chrysarobin or potassium permanganate, for the lesions were either macerated or stained, showing some use of these agents. In the case presented, the patient was careful and wanted to get well. She carried out the treatment thoroughly with copper sulphate, and the lesions healed entirely. Two other patients had made great improvement under treatment with wet dressings of copper sulphate. In other cases, it might be that tincture of iodin or chrysarobin or Whitfield's ointment would lead to cure. He wished to modify his statement concerning the marked resistance to treatment by saying that the first patient may not have carried out her treatment properly.

DERMATITIS EXFOLIATIVA. Presented by DRS. ORMSBY and MITCHELL.

A woman, aged 36 years, stated that she had suffered with mycosis fungoides for several years and had been treated successfully for that disorder. Four months before, she was persuaded to take the so-called Abrams' treatment. This included injections of a so-called serum. Shortly after these injections the present symptoms developed. The entire cutaneous surface became red, swollen and edematous. This was followed by general scaling. The scales varied in size at different times.

When first seen, the entire surface, including the scalp, was erythematous and covered with scales. The ankles were edematous. The abdomen was distended and examination revealed much fluid. The pericardium likewise contained fluid. The entire cutaneous surface was constantly moist from exuding fluid. The blood findings showed signs of anemia. Hemoglobin was 60 per cent.; red cells, 3,410,000; white cells, 9,600. The urine was normal, except that it was reduced in amount. (A chemical examination for arsenic was negative.) The fluid intake was ten times greater than the urinary output. No sensation other than chilliness was present.

DISCUSSION

DR. ZEISLER said that he had taken care of this patient for about nine years. She had had typical mycosis fungoides but was kept comfortable by roentgenotherapy. During the last year, she became worse under this treatment and arsenic, but she had never shown any symptoms of exfoliative dermatitis. At present she had symptoms of generalized exfoliative dermatitis and was water-logged.

DR. ORMSBY said he believed that it might be of interest to state that when this patient was given the Abrams' treatment she was not in a very bad condition, but she had had the trouble for a long time and was persuaded to take the injections. Knowing that arsphenamin produced such an eruption, he sent an inquiry to the physician concerning the character of the treatment. He replied that he would not use arsphenamin, and that he had employed "autohemic" treatment. The woman had ascites, and her intake of fluid was ten times as great as her output. Her urine was reduced, but her body was constantly bathed with fluid, so that evidently the fluid that was lost was excreted in that way. Her entire body was involved in the dermatitis, with the exception of about 4 square inches.

A point to consider was whether the condition might be an erythroderma as a part of her mycosis fungoides. Her blood picture showed nothing at present. He supposed the "autohemic" injections could not produce the condition, but he thought it strange that it appeared so soon after the injections were given. The chemist could find no trace of arsenic in the urine now.

DR. STILLIANS said the treatment was originated by a quack in Chicago who was willing to teach the method to any one for a consideration of several hundred dollars. So far as known, he took a small amount of blood from the patient, separated the serum, heated it and then diluted it greatly and injected a small portion intravenously. Whether this would cause a violent toxic disturbance or not, he did not know.

DR. ENGMAN said he was once much distressed by a patient who was treated by the Abrams' method, because the physician who treated this patient had thoughtlessly pushed the wrong button. He pushed the tuberculosis button, when the patient had syphilis.

LUPUS VULGARIS. Presented by DRS. ORMSBY and MITCHELL.

A youth, aged 16 years, who had had lesions on the neck, left arm, hand and both feet since 2 years of age, had lesions which began as a "boil" on the left foot; the bones then became involved, and an operation was performed. Subsequently, the bones about the left hand and wrist became similarly involved, and in 1915 another operation was carried out. Since that time the left elbow had been fixed at a right angle. At the time of presentation, there was a small active sinus in the left hand.

The patient had received roentgen therapy, and later radium was administered. About one year ago, he was given a series of intravenous injections, probably of arsphenamin. These were followed by intramuscular injections, possibly of mercury. No history of tuberculin injections could be elicited.

When presented, there was a typical area on the right side of the neck which extended from the lobe of the ear to the clavicle and from the midline in front to the midline on the nucha. There was also a large area on the ulnar side of the left hand, which involved both the dorsal and palmar surfaces. There was a small sinus at the base of the left little finger. There was a large area of scarring and bony deformity in and about the wrist. There was a large patch on the lower outer surface of the left upper arm and scattered nodular patches on the left forearm. Various bony depressions were present about the dorsum and ankle of the left foot, and there was a large area covered with silver scales on the posterior half of the sole and heel of the left foot.

A CASE FOR DIAGNOSIS. SPRUE (?). Presented by DR. RAVITCH.

A boy, aged 11 years, consulted his family physician in December, 1919, because of herpetic lesions in the mouth. The lesions were cauterized, with unfavorable results. A Wassermann reaction at that time was said to be faintly positive, but subsequent tests were all negative. The patient was given intense arsenical and mercurial treatments, without results. His condition had grown worse in the last year, and he had been referred to Dr. Ravitch several weeks previously by a pediatrician, who claimed that similar lesions were found around the rectum, which disappeared on withdrawal of carbohydrates from the diet and the addition of plenty of vegetables and fruit juices. Smears and sections were taken from his mouth for examination, with negative findings, except for a few *Monilia albicans*. Sprue was suspected.

DISCUSSION

DR. LAIN said that he was reminded of a case he had recently seen, in which an accurate and yet, at the time, seemingly far-fetched diagnosis of pemphigus was made by Dr. Stokes and Dr. Goeckerman. This patient had

visited the Mayo Clinic twice, and the second time the diagnosis of pemphigus was made with no lesions present except those on the mucous membrane. Dr. Lain was sure the diagnosis was correct and thought the lesions in this child's case suggested the same diagnosis. The cultures had been negative in the case he referred to.

Dr. Driver said he was interested in the case because of the possibility of erythema multiforme. He asked whether salicylate had been used in the treatment.

Dr. Cole said he had not thought it was a case of erythema multiforme but considered the suggestion good.

Dr. Weiss asked about the possibility of scurvy in such cases.

Dr. Eisenstaedt said that he saw this patient seven or eight months before, when he was under the care of Dr. Abt. The pediatricians went over the case from every possible angle but could arrive at no diagnosis. The only positive finding at any time was shortly after his entrance to the hospital when the organism of thrush was found. Treatment had apparently been of no avail, and no improvement had occurred. The condition had been present for three years, going from bad to worse. There were no lesions about the rectum when he saw the child, although there was a history of similar lesions in that locality. There was distinct loss of mucosa with an exudate down to the gingival margin and involving that, also on the buccal mucosa.

Dr. Zeisler asked whether it could be an infection with an organism of the monilia group.

Dr. Ravitch said that the same lesions were found around the rectum, but on the carbohydrate-free diet and fruit juices those lesions had disappeared, while those in the mouth had persisted. No definite diagnosis had been made, but some pediatricians believed it was a case of sprue.

GRANULOMA PYOGENICUM (RECURRENT). Presented by Dr. Zeisler.

A boy, aged 7 years, whose disorder had been present for one year, had a pedunculated vascular nodule on the back of the neck, which had been removed twice and had recurred each time. The histology was typical of granuloma pyogenicum.

Specimens were shown under the microscpoe.

PROGRESSIVE IDIOPATHIC ATROPHY. Presented by Dr. Waugh.

A woman, aged 40 years, who had worked in factories for many years, had a disorder which had been present about two years, beginning on the lower extremities and later involving the hands and arms. The skin presented a bluish red atrophic and wrinkled appearance, with slight brainy scaling in places. Practically no subjective sensation was present.

DISCUSSION

Dr. Eisenstaedt called attention to the marked injection of the conjunctivae and asked whether this was a part of the condition.

Dr. Waugh said he believed that the conjunctivitis was not a part of the disorder. The woman did a great deal of hard work in dusty factories, and he considered the eye condition due to mechanical irritation.

He thought the blood picture was of special interest and said that the patient was shown in Dr. Herrick's clinic, where a careful blood examination was made and an extremely marked polycythemia was found, the red count being eight to eleven million and the hemoglobin about 70 per cent. The medical staff was much surprised in reading the laboratory findings on the blood. The patient had improved considerably on potassium iodid treatment. Dr. Waugh thought it might be of interest to know that the medical men had endeavored to find a disturbance of some of the glands of internal secretion, but they had not arrived at any definite conclusion.

LUPUS ERYTHEMATOSIS OF THE SCALP. Presented by DR. STILLIANS.

An American school teacher, aged 31 years, in March, 1922, first noticed two dime-sized bald spots. Since then four others had appeared. There was no sensory symptom.

Examination showed sparse hair, characteristic of seborrheic alopecia. There were six completely bald spots, without scales of broken hairs, 0.5 to 1.5 cm. in diameter. The skin of these spots was smooth and contained many telangiectases. The largest of these areas was slightly depressed below the general level of the skin. Under the diascope the skin looked white, with many brown spots corresponding to the follicles.

RAYNAUD'S DISEASE. Presented by DR. WAUGH.

A man, aged 31 years, whose disorder was of five months' duration, first noticed a temporary ischemia of the skin when his hands were placed either in cold or warm water. The color was quite pale, and the hands were lifeless in appearance; this condition would persist for ten or fifteen minutes, when the normal color would return. During the last five months, superficial painful erosions had appeared on the tips of several fingers.

DISCUSSION

DR. WAUGH said the case was interesting because of the rapidity with which the disease had developed. The man had come into the clinic recently after he had noticed for a short time that on placing his hands in either hot or cold water they would become like the hands of a corpse within a few minutes. This feeling persisted along the course of distribution of the ulnar nerve for half an hour. An internist saw the man with him and suggested the possibility of Raynaud's disease at that time. The patient soon developed the painful ulcers over the tips of the fingers. The patient had incised one or two of them, thinking there was retained pus because of the pain.

NEUROTIC EXCORIATIONS. Presented by DR. JACOBSON (by invitation).

A Polish laborer, aged 36 years, had a disorder which had been present for two years. It began as an itching sensation all over the body. He received internal medication, but the itching persisted, appearing in one place on some occasions and at other times in several places; it would remain for a minute or two, then suddenly disappear and reappear in different spots. When general, the itching was often accompanied by chills. The skin would feel hard in places, and the patient had been in the habit of rubbing raw potatoes over the itching areas, which relieved the sensation somewhat. He said that he had noticed peculiar sounds in the skin at different places; these sounds

would come on three or four times a day, sometimes once a day or once in two or three days. He complained also of a painful tongue. The joints on moving had a cracking sound. He had been scratching himself, leaving scars all over the body, especially on the hands, face and legs.

The patient denied venereal disease. He had been troubled with vomiting and sour stomach, without relation to the taking of food, for the last two years and was bloated at times. He had had some diarrhea and nocturia for two or three weeks.

DISCUSSION

DR. PUSEY said he believed this was a case of neurotic excoriations.

CHRONIC ULCERATING GRANULOMA OF GROIN. Presented by DR. OLIVER.

A man, who was presented at the annual meeting in 1922 (reported in ARCH. DERMAT. & SYPH. **5**:790 [June] 1922), with an extensive ulcerating granuloma which involved the abdominal wall, groin and penis, while in military service in Italy had been cut and torn by contact with barbed wire entanglements, and the wounds had become infected. Smears were negative for Donovan bodies and Ducrey bacilli; the Wassermann reaction was negative. The condition resisted all treatment, including prolonged immersion in water, cauterization, curettage, injections of arsphenamin and tartar emetic, iodoform and argyrol applications. On Oct. 25, 1922, the lesions were covered with full strength radium plaques screened with rubber, which were allowed to remain for twenty minutes. Considerable reaction occurred, but there was marked improvement. This treatment was repeated on December 8, and the patient was presented to show the results of radium therapy.

DISCUSSION

DR. STOKES said he believed the radium therapy which achieved such an exceedingly successful result in this case should be credited to Dr. Irvine. Dr. Irvine had suggested to him that the effect of very small doses of radium might be beneficial in the case Dr. Stokes presented at the annual meeting in 1922. Consequently, he used a 20 mg. plaque, two minute applications around the lesion, and to his astonishment the lesion healed. If this was a real contribution to the therapy of these exceedingly persistent ulcers, the credit should certainly go to Dr. Irvine.

DR. WAUGH said he had had a similar case last summer. A man with a definite syphilitic history developed an ulcer on the left thigh about six months after the primary lesion. This progressed to the size of a dinner plate. Arsphenamin and mercury had no effect on this large ulcer, although the other symptoms of syphilis cleared up. The ulcer was dark red, quite painful and tender. The patient was put on tartar emetic intravenously, beginning with $\frac{1}{6}$ gm. and increasing to 1 gm. every other day. He received thirty-five injections, and when last seen the ulcer had healed at least 50 per cent. The patient had returned home, but Dr. Waugh thought there was no doubt that the tartar emetic therapy had helped.

DR. OLIVER said that this man was shown last year and up to October 25 the ulcer was still open. He was put in a warm continuous bath and given arsphenamin, tartar emetic, and an iodoform pack was used in the ulcers. At the October meeting of the Society he talked with Dr. Stokes, who gave him

the valuable suggestion from Dr. Irvine concerning radium therapy. Following that he used a full strength radium plaque for twenty minutes. There was a definite response to this treatment, and a remarkable improvement followed. He felt that the credit was due to Dr. Stokes and Dr. Irvine.

EPITHELIOMA ON LUPUS VULGARIS SCAR. Presented by DR. WAUGH.

A man, aged 49 years, had a scarring lesion which had been present for forty-five years. The lupus vulgaris had been most acute during childhood and youth and had been treated in several of the German clinics. The lesion, which was active at the time of presentation and the size of a half dollar, began as a small papule in the center of the lupus scar eight months previously and had gradually increased in size. The family and personal history were negative with the exception of this disorder.

The patient had received two erythema units of roentgen-ray ten days before.

DISCUSSION

DR. WAUGH said the case was interesting because the lupus was still active after forty-five years and because of the development of the epithelioma on the lupus scar. The patient had received one treatment with the roentgen ray, 2 units having been given about ten days previously, which had reduced the lesion fully 50 per cent.

A CASE FOR DIAGNOSIS. Presented by DR. WAUGH.

A Russian girl, aged 17 years, whose disorder was of one year's duration, complained of pain and tingling at times in feet and hands and of an eruption which was aggravated during cold weather. Most of the lesions were papules and nodules; at times a few vesicles would appear on hands and fingers. The skin of the feet, legs, hands and arms was bluish-red. The ears were not involved. The Wassermann reaction was negative; the family history was negative, except that the patient was ill for three weeks four years ago with what was said to be typhoid fever.

DISCUSSION

DR. FOERSTER said he believed it was a case of lupus pernio or lupus erythematosus.

DR. GRINDON said he believed one should know the girl's condition as a whole. In speaking of lupus pernio, a French writer says these patients are "fish-like individuals," or, as our fathers would have said, of a lymphatic temperament. This patient's feet were cold; there was marked venous congestion of her legs and a slow circulation. She was just the type of person in whom one would look for lupus pernio. From the appearance of the girl's finger tips alone, he would have called it a case of lupus erythematosus, but the forearm patches were rather more like lupus pernio.

DR. LAIN said he was particularly interested in this case, first because of the dermatologic phase, but more especially because of the possible etiology. The girl was anemic and had a rather septic appearance which suggested the possibility of some septic process. He had noticed several carious teeth, and in addition to that the tonsils were greatly enlarged and there was cervical adenopathy, both deep and superficial, on both sides of the neck. He believed that there might be some localized foci of infection as an etiologic

factor. He had seen patients with similar cases show marked improvement or recovery under ordinary methods of treatment when these lesions were taken care of.

DR. LIEBERTHAL said that he saw this patient six months before. At that time the forearms were involved, showing deep blue discolorations, but there were no lesions on the fingers. He would have expected the condition to disappear during the summer and to appear during the winter, but this was apparently reversed. The lesions on the fingers, the papulonecrotic lesions, were unquestionably of a tuberculous nature.

DR. RAVITCH said that he could understand the girl because he spoke Russian. She was extremely nervous and said that she had had the disease for more than a year.

DR. WAUGH agreed with the diagnosis of lupus pernio. He thought some of the members would recall a patient shown two years ago at the annual meeting, a young man who presented an atrophy of the lobes of both ears with discoloration of the nose and of the hand. He also had two patches of lupus erythematosus on the face and presented the plaques on the hand, but not a vesicular eruption such as this girl had. On the lower extremities the condition was much more marked than on the upper extremities in the present case. When she came to the clinic, there was a peculiar mottled appearance almost to the waist line.

PAGET'S DISEASE. Presented by DR. MCEWEN.

A woman, aged 40 years, whose disorder was of seven years' duration, said that when first noticed there was present a small scale covered area about the size of a ten cent piece. This had enlarged gradually by peripheral extension to the size of half a dollar. The lesion was rather dark red, always dry, scale covered and the margin slightly elevated. The family and personal history and the Wassermann reaction were all negative. A biopsy confirmed the diagnosis of Paget's disease.

DISCUSSION

DR. WILE said he believed it was undoubtedly an example of Bowen's type of epithelioma. Some of the sections did not show any carcinomatous infiltration, but Dr. Butler and one or two others, including himself, found definite carcinomatous infiltrations.

DR. WAUGH said there was no question about the case being one of Paget's disease.

DERMATITIS REPENS. Presented by DRS. ORMSBY and MITCHELL.

A man, aged 30 years, whose disorder had been present for eight years, had been presented at the last three annual meetings of the Chicago Dermatological Society and was shown again at this time to demonstrate the slight change in the condition in spite of constant treatment during the year.

DISCUSSION

DR. GRINDON said that he had been successful in the treatment of some of these cases with Stelwagon's treatment, 10 grains of resorcinol to an ounce of saturated boric solution, mopped on freely for ten minutes at a time and then dusted with boric acid.

CHICAGO DERMATOLOGICAL SOCIETY

Regular Meeting, Feb. 21, 1923

EDWARD A. OLIVER, M.D., *Presiding*

PARAPSORIASIS LICHENOIDE (BROCQ). Presented by DR. WAUGH.

A man, aged 30 years, who had been seen by Dr. Waugh the first time the day before presentation, had an eruption which first developed on the arms, legs and thighs six months before, and more recently in the lumbar region. He had been in the Soudan region of Africa for three years previous to six months ago. The lesions had persisted since their appearance without any cessation. There was no subjective sensation. The eruption was of retiform character: the lesions being mostly pea or dime size, flat, slightly scaling, some faintly pink, others a pinkish yellow or almost the normal color of the skin.

DISCUSSION

DR. MCEWEN said he believed it was a case of parapsoriasis.

DR. FOERSTER said he believed it was an example of the pityriasis lichenoides chronica (Juliusberg) type of parapsoriasis. There were a number of papules and a peculiar collodion-like scale.

DR. SENEAR and DR. MITCHELL agreed with Dr. Foerster.

DR. WAUGH said he was interested in the rapid development of the disorder and the spreading over the trunk and extremities. He asked for suggestions as to therapy that might be beneficial, and recalled a case that was under Dr. Ormsby's care several years ago, in which nothing seemed to have any effect.

DR. MITCHELL asked whether Dr. Waugh remembered the effect neorobin had in that case. The result of treatment with this preparation was apparently remarkable. The patient was to come in to have a photograph taken to show the cure, but when he reappeared his condition was just the same as before.

DR. FOERSTER said he had heard that such cases of Brocq's erythroderma were treated with the Alpine lamp, with good results.

He called attention to the fact that the man had a supernumerary nipple and said that when he was on a medical advisory board and examined 2,980 drafted men, he found seventy-one with supernumerary nipples, of which six were multiple, and the remainder single.

EXTRAGENITAL CHANCRE. Presented by DR. SENEAR.

A man, aged 42 years, a farmer, late in December, 1922, burned his tongue with a hot spoon. He said that the tongue was denuded over a considerable area. One week later, a nodule appeared on his tongue, reaching its greatest size within a short time. Since then it had gradually decreased in size until it was about half its original diameter. There had been no glandular enlargement. The lesion was painless. About ten days before presentation, he developed a maculopapular eruption over the upper part of the body, unaccompanied by pruritus. The Wassermann reaction was reported strongly positive on February 10. There was no previous history of syphilis, but he had had an attack of gonorrhea twenty years before. There had been no exposure through intercourse for three years, but early in January he attended a party where kissing games were played. The man had burned his tongue in eating

an oyster from a spoon in which it had been cooked and about ten days later attended a "kissing party." The chancre developed one week after this exposure.

DISCUSSION

Dr. McEwen said he believed it should be borne in mind that it was possible that neither the oyster, the spoon nor the kissing was the source of the infection.

Dr. Foerster was interested in the fact that the lesion was on the dorsum of the tongue, half an inch (1.27 cm.) back of the tip. It was an unusual location for a lingual chancre, and he believed the injury had something to do with providing the site for the lesion. Ordinarily, lingual chancres are found on the tip of the tongue.

Dr. Mitchell said they had recently seen a man aged 84 with a primary lesion on the tip of the tongue. He had made a practice of kissing every woman or girl who would permit it.

CONGENITAL ICHTHYOSIFORM ERYTHRODERMA. Presented by Dr. Oliver.

An infant, aged 4 months, weighed 9 pounds and 11 ounces (4.4 kg.) at birth. The skin was red, shiny and scaling, the hands flexed and the fingernails clawlike. The epitrochlear glands and spleen were not palpable. The Wassermann reaction was negative on the blood. The mother's blood Wassermann reaction was negative; the spinal fluid Wassermann reaction with cholesterolized antigen was ++++; the Lange and globulin tests were negative; there were 13 cells.

DISCUSSION

Dr. Foerster said he believed it was a case of ichthyosiform erythroderma, and said the mother's hands were distinctly hyperkeratotic.

Dr. McEwen agreed with Dr. Foerster, but he said that he was impressed with the fact that this case was a case in which incompetent diagnosticians had rushed to the treatment of syphilis on insufficient evidence and had thereby brought about complications in the matter of making a correct diagnosis which would require a long time to remove. He was encountering these cases of wrongly diagnosed "syphilis" constantly and thought the situation had a distinctly serious aspect.

Dr. Oliver said the syphilis department had never been in the hands of the dermatologists at the Children's Hospital. He did not see the child under discussion until it had been under treatment for two months. He understood the diagnosis of syphilis had been made on the appearance of rhagades about the mouth and the exfoliation of the palms and soles, rather than on any conclusive evidence.

IDIOPATHIC MULTIPLE HEMORRHAGIC SARCOMA (KAPOSI). Presented by Dr. Waugh.

An Italian, 73 years of age, had lived in America for thirty-seven years. His disorder had been present for about two years. A vesicular eruption was first noticed on both lower extremities; about one or two months later the bluish red, nodular lesions developed. There were about 100 on each leg

between the knee and the ankle, principally on the anterior surface. Subsequently, lesions appeared on the arms, chest and thighs. None of the lesions had disappeared. They had always been painless; most of them were about the size of a pea, although a few were larger. The skin below the knees was hard, infiltrated and more or less edematous. The lesions on the arms were discrete, elevated, rather dark red, infiltrated areas; fifteen of these lesions which were slightly scaling were situated on the left arm and hand. There was no subjective sensation.

DISCUSSION

DR. MCEWEN said he believed the condition was Kaposi's sarcoma.

DR. MITCHELL said this was his impression from the clinical picture, particularly the lesions on the legs.

DR. FOERSTER said he had not seen the sections, but he believed it was a case of multiple hemorrhagic sarcoma.

DR. WAUGH said he believed there was no question about the correctness of the diagnosis. The sections he showed were secured from a lesion that had been present for a little more than a year, and he had not secured a section from a later lesion. The section presented corresponded quite well with the condition as described. The elastic tissue was practically absent, and the blood and lymph spaces greatly dilated with intracellular infiltration around the vessels. There was not as much round cell infiltration as in some instances, and he said he would make an effort to get another section from the lower extremity. Dr. Ebert had been doing histological work.

EROSIO INTERDIGITALIS SACCHAROMYCETICA. Presented by DRS. SENEAR and WIEN.

A woman, aged 56 years, about eighteen months before presentation injured the skin in the fourth interdigital space with a nail. The wound healed in about five days. About six weeks later she noticed a small lesion from which she squeezed water. This disappeared, but it recurred at intervals until two months ago, when the skin became macerated and red and caused some distress.

A 2 per cent. solution of copper sulphate, as advised by Dr. Mitchell, was employed, and improvement was rapid until about one week before presentation, when the condition again became acute.

DISCUSSION

DR. MITCHELL said this case was not as well defined as usual, but this was probably due to the fact that the lesion had largely cleared up.

DR. SENEAR said that when he first saw the patient she had the characteristic lesion with the overhanging edge about it. This had nearly cleared up under treatment. He was interested in the therapeutic effect. The copper sulphate had worked well, in spite of the fact that there had been some recurrence, which he thought was due to the fact that the patient had her hands in water much of the time.

DISSEMINATED SCROFULODERMA. Presented by DR. OLIVER.

A boy, aged 11 years, had had the disorder for three years. The eruption extended over the face and body.

DISCUSSION

Dr. Foerster said he had made a diagnosis of scrofuloderma, but, he thought the condition could very well be taken for syphilis. He believed, however, that all other disease processes could be ruled out, and that the diagnosis would lie between tuberculosis and syphilis. He was in favor of tuberculosis, largely because of the peculiar scar with a bridgelike formation on the left cheek, and he believed no condition except scrofuloderma produced the kind of bridgelike scarring with an overhanging of the margins, that was present here at both the upper and lower borders.

Dr. Pusey said he was inclined to think it was a case of syphilis. Part of it was superficial in the subcutaneous tissue; it had a striking tendency to annular arrangement, and it did not correspond to the picture of the annular lupus which is sometimes seen. He agreed that the lesions on the cheek were like those of scrofuloderma, but those on the arm did not look like scrofuloderma or like lupus. As Dr. Foerster had said in talking over the case, it was easy for syphilis to simulate tuberculosis but hard for tuberculosis to simulate a syphilid, and he thought the boy had syphilis.

Dr. McEwen said he did not think it was syphilis, because of the hypertrophic type of scarring and because, were it syphilis, probably during the three years' duration there would have been some period when it would have been more or less healed. The boy looked healthy, did not have the teeth of a congenital syphilitic and did not give a history of eye trouble. He did not consider it a case of scleroderma but believed it was of tuberculous nature. In his opinion, blastomycosis would have to be excluded carefully.

Dr. Senear said that when he looked at the lesion on the arm mentioned by Dr. Pusey, he thought it was a case of syphilis. Then Dr. Foerster called his attention to the bridgelike scar, but he was still more inclined to a diagnosis of syphilis. He could not see any typical yellow color, but there was some slight suggestion under the diascope.

Dr. Oliver said he had seen the patient only once before, but he thought the case so interesting that he presented the boy for the consideration of the Society. His impression was that it was a tuberculous condition of some type, but he was openminded, and he would have a Wassermann test made. (Since the last meeting the Wassermann test had been made and found negative).

Dr. Mitchell said he believed if one were looking at the lesion on the right arm in a moulage without knowing anything about the case one would accept it as syphilitic, and this was also true of the one over the right nipple. As to the appearance of congenital syphilis, the boy had no more signs of pulmonary tuberculosis than of syphilis. He might have acquired syphilis. He had seen such cases from time to time, and they had histories in the office of quite a number of acquired cases in children. The lesion on the left arm might well be a mycotic process, but those on the right chest and right arm were difficult to differentiate from syphilis.

Dr. Oliver said the lesion on the right cheek was soft and velvety, with no suggestion of syphilis. The patient had used ointments prescribed by the family physician.

Dr. Eisenstaedt said he felt much as Dr. McEwen did, that the case was of tuberculous nature, but he did not exactly follow the definition of scleroderma. The large, hypertrophic scar was suggestive of blastomycosis with the peculiar puckering, and he agreed that this would have to be ruled out.

A CASE FOR DIAGNOSIS. Presented by Dr. Senear.

A girl, aged 17 years, presented an eruption which had been present on the trunk and extremities for the last eighteen months, varying in intensity but never clearing up entirely. Itching was severe at times, and the intensity of the eruption and the itching were greater at night.

On the trunk and extremities was a generalized eruption of annular, reddish-brown lesions, varying from the size of a split pea to that of a half dollar. Many of the lesions were slightly elevated and covered with thin, adherent scales. There was no dermatographism. The patient had "chilblain circulation" with livedo reticularis of the arms and legs.

DISCUSSION

Dr. Waugh said he did not think the case was a seborrheic dermatitis or chronic urticaria, but he did not know what it was.

Dr. Pusey said he thought it was necessary to exclude a seborrheic dermatitis, but he did not know what the condition was.

Dr. Ravitch suggested tricophytosis.

Dr. Foerster said there was evidently some follicular involvement, but he did not know what it was.

Dr. Mitchell said that if he might be permitted to coin such a phrase, the case suggested an unresolved pityriasis rosea.

Dr. Senear said he was interested in Dr. Mitchell's suggestion because some cases of "unresolved pityriasis rosea" had been reported, but he thought the distribution did not look like that disorder. He had recently read the report of a case of tricophytosis that was similar to this, and the patient afterward developed typical tricophytosis cruris. He had tried to secure some scales from the lesion, but it had been impossible to do so.

Two or three years ago, Dr. Pusey and he had a case somewhat like this one, and Dr. Foerster suggested at that time that it was an urticarial type of dermatitis herpetiformis, which proved to be correct. The picture in this case did not look like that, but because of the intense itching he had thought of that possibility.

TUMORS (?) Presented by Drs. Senear and Weber.

A colored girl, aged 17 years, for the last few years had noticed small tumors appearing over the trunk and hips. No subjective symptom was complained of.

Over the trunk and upper part of the arms were a number of tumors varying in size from that of a split pea to that of a walnut. They were soft and readily reducible through a hernia-like opening in the skin. Over the upper part of the trunk, there were a number of flattened, slightly elevated patches, which had not as yet assumed the round or oval dome shape of the tumors.

DISCUSSION

Dr. Foerster said he thought it was an example of Buzzi-Schweninger type of tumor formation, to which Dr. Pusey had called attention in this country. The distinctive lack of resistance of the skin to pressure as observed in this condition, was pronounced in Dr. Senear's patient. The fact that it occurred in a colored person was of interest. Dr. Foerster said he did not recall having seen the disorder reported in the literature as occurring in other than white patients.

DR. MITCHELL said he believed Dr. Foerster was probably correct in his opinion. The lack of resistance was against the diagnosis of Recklinghausen's disease, although the pigmentation was rather characteristic of the disorder suggested.

DR. PUSEY said that at the time he reported his case two years ago there was only one case of the Buzzi-Schweninger type in the literature, and he believed there were few at the present time.

DR. SENEAR said he thought it was a multiple benign tumorlike new growth. The lesions over the shoulders were much like those in Dr. Pusey's case. He had thought of Recklinghausen's disease because of the pigmentation, and because the patient was not very bright; a sister three years younger was much brighter. A similar case had been presented in New York as a Buzzi-Schweninger type, and Recklinghausen's disease had been taken into consideration. Several members commented on the lack of pedunculation, stating that the latter was not necessary in Recklinghausen's disease. He said he would make a further study of the case and report later.

DR. OLIVER said he had a girl under observation who had one large tumor on the heel, and she was now developing areas of pigmentation. Dr. Finnerud had seen the patient, and a diagnosis of Recklinghausen's disease had been made.

DR. MITCHELL said that in his war work he saw many cases of Recklinghausen's disease, and he had found that lowered mentality was not often associated with the condition.

DR. WAUGH said he thought it was a case of Recklinghausen's disease with the typical areas of pigmentation and the soft tumors.

A CASE FOR DIAGNOSIS. Presented by DR. SENEAR.

In a colored boy, aged 7 years, lesions had appeared on the arms, legs and trunk ever since infancy, always being more numerous in the spring and summer. The patient said that there was no itching, but the father said that during infancy it had been necessary to tie his hands to prevent scratching, and that he still scratches the lesions at times.

The trunk and extremities were covered with a number of pinhead to split pea sized papular lesions, some with vesicular or crusted centers. A number of superficial scars were present as a result of the involution of old lesions.

The Pirquet test was positive, while roentgen ray and physical findings in the chest were suggestive of tuberculosis.

DISCUSSION

DR. STILLIANS said he thought the condition was a papulonecrotic tuberculid.

DR. PUSEY agreed.

DR. MITCHELL said he could not come to any conclusion. The lesions were rather suggestive of lichen urticatus. If the patient had had any vesicular patches from time to time, he believed it might be that disorder, particularly as it was aggravated in the spring and summer months. Aside from that, he could come to no conclusion. It might be dermatitis herpetiformis, although he had never seen that in a negro.

DR. WAUGH said he thought it was lichen urticatus, and he believed the skin was more likely to show infiltration in the colored race in such cases than in the white.

Dr. Senear said that the apparently positive findings of tuberculosis reported by the pediatric department made him think that it might be a tuberculid. The first time he saw the patient the lesions were capped with a white vesicle. The intense pruritus and seasonable exacerbation seemed to suggest lichen urticatus. The scarring, which was rather more extensive than usual in such cases, might have been the result of scratching.

NEW YORK DERMATOLOGICAL SOCIETY

Regular Meeting, Jan. 23, 1923

W. B. Trimble, M.D., *President*

POIKILODERMA ATROPHICANS VASCULARE. Presented by Dr. H. H. Whitehouse.

S. M., a woman aged 34, married, Bohemian, a housewife whose father and mother, two brothers and and six sisters were living and well, said she had never had any diseases. She began menstruating at the age of 18 and menstruated regularly every three weeks. She married at the age of 21, and had never been pregnant.

Her present condition began thirteen years ago on the anterior surface of the right shoulder as a small area about 2 inches (5.08 cm.) in diameter. From the patient's description, it was similar to mycosis fungoides. Several months later the lesion became larger, showing some reticulation, telangiectasia and areas of atrophy resembling a roentgen-ray dermatitis. Eight years later other similar lesions appeared on the chest, abdomen and back, going through the same process as the previous one on the shoulder with more marked atrophy, pigmentation, reticulation and telangiectasia. The condition covered the greater part of the chest, abdomen and back, with the exception of an area about 2 inches in diameter around the nipples and a small part around the navel, which was normal. There were two areas on the back over the scapulae, about the size of a hand, which were red and scaly and showed more telangiectasia and atrophy than any other area on the patient's body. The reticulation was not plain. The most typical areas on the anterior surface of the body were above and below the breasts, and were about the size of a palm. Atrophy, telangiectasia and retriculation were definite here. The patient had had an ulcerated area about 2 inches wide and 3 inches (7.62 cm.) long on the right side of the neck, for the past three years. The ulcer had a smooth, shallow base, thin ragged edges, not indurated, and it healed under ichthyol ointment. About a year ago, lesions appeared on the arms and legs, which resembled mycosis. These became red and indurated, and in a few days faded, leaving pigmentation, and recurred at short intervals. The face and mucous membranes were free, as were also the palms and soles. There were symptoms of burning and soreness, particularly in the larger patches.

The patient was healthy, about 5 feet, 8 inches (172.72 cm.) tall, and weighed about 140 pounds (63.5 kg.). She seemed more or less depressed at times. She said that ten years before, in Budapest, all the patches disappeared within two weeks following the use of some drops.

Biopsy: There was marked acanthosis with papillary prolongation of the derma, extending almost to the horny layer, which showed increased vascularity

with some small round cell infiltration, which was also present in the superficial derma. There was some pigment in these regions. The stratum granulosum was prominent, and there was some parakeratosis with moderate hyperkeratosis. If mycosis fungoides, the process was at a stage before there was thinning of the epidermis from pressure.

Roentgen-ray examination revealed a normal chest and pituitary body. The urine analysis and blood count showed no abnormalities. Chemical analysis of the blood revealed 100 mg. of glucose per 100 c.c. of blood, 0.47 mg. of creatinin, 4.3 mg. of uric acid, and 7 mg. of urea nitrogen.

The patient was in the hospital for thirteen weeks, leaving on Aug. 19, 1922. Since her discharge she had received roentgen-ray treatment every fortnight, applied to the back and neck, without any apparent effect. There had been four such applications.

DISCUSSION

Dr. Lane said that with the small number of cases so far reported it was impossible to draw a sharp line as to what should be included under the name of poikiloderma. There was great variation in appearance, and while this case was markedly different in many respects from his own, he felt that it was nevertheless an example of poikiloderma. As compared with his patient, there was here much less pigmentation, atrophy, and telangiectasia, while the inflammatory signs were greater. The reticulation so often noted was present here only about the breast.

Dr. Highman said it was a privilege to have had the opportunity to see so remarkable a case. He imagined that histologic study would show an inflammatory process in the capillaries and destruction of the elastic tissue, a group of changes suggestive of what occurs in typical discoid lupus erythematosus.

Dr. Lane replied that the histologic examination had shown two stages of the disease, an inflammatory and an atrophic. The inflammatory stage was manifested by perivascular round cell infiltration and dilatation of the superficial vessels, and alternate increase and diminution or absence of pigment; the atrophic stage by flattening of the papillae, degeneration and disappearance of the elastic tissue and atrophy of the collagen bundles. The histologic report given by Dr. Whitehouse fitted as a description of the inflammatory stage of the disease, and the clinical appearance of most of the lesions in this case indicated that such was the case.

Dr. Highman said that with the clinical picture of poikiloderma went the pathologic picture seen in essential telangiectasia plus the atrophic changes of scleroderma. Clinically, the case suggested a relationship with lupus erythematosus, although telangiectasia was more marked, while some of the lesions suggested the fixed erythema group. It would be interesting to know whether poikiloderma might not be classified as a fixed erythema going on to more marked atrophy than is usually observed in erythema perstans. This might be a process leading to a final picture more distinctly advanced than that seen in erythema perstans. It was unique, and from its distribution one would expect a toxic process or a focal infection to explain it. This disease was closely related to the other essential telangiectasia, such as purpura annularis, angioma serpiginosum, and similar diseases.

Dr. Wise said that the two cases that he had seen were much more advanced. Dr. Lane's case showed advanced atrophy, and there were also ulcerations. He believed that the diagnosis as presented was the most likely one, as other diseases could be excluded.

Dr. Howard Fox said that from his recollection of the subject, cases of this disease resembled roentgen-ray burns with telangiectases, pigmentation, etc. As this patient showed no pigmentation, it was not the picture of a roentgen-ray burn, and in that respect did not accord with the description of the disease. He thought the suggestion of lupus erythematosus should be seriously considered.

Dr. Whitehouse said that the diagnosis might well be accompanied by a question mark; some of the features varied so from those of cases that had been reported that it was hard to be dogmatic. One of the anamnestic features of this case, if true, was interesting and was not evident in any of the others; namely, the patient's statement that in Budapest, ten years ago, it entirely disappeared in two weeks while she was taking some drops. So far as he understood, poikiloderma was a progressive disease and never disappeared. This patient had the ulcer on the neck which had lasted for two years—whether it was due to traumatism or not, he did not know. As to the subjective symptoms, she had the same dryness of the skin to which Dr. Lane had referred, and was very uncomfortable unless it was kept greased, but it lacked the essential pigmentation shown in most such cases, and the distinct well marked features of a roentgen-ray atrophy. It was his intention to study the case further, and he hoped to be able to make a further biopsy. With regard to the discussion of the other reported cases, as Dr. Lane had brought out in his paper and during the discussion that followed, it was considered very probable that poikiloderma was of toxic origin. Some likened it to diffuse idiopathic atrophy, and there was much difference of opinion. Lupus erythematosus as a possible diagnosis was mentioned by some. The condition did not seem to have anything to do with Majocchi's or Schamberg's disease, as persons with both of those recovered, while those with this disease did not.

Dr. Highman asked what finally happened to poikiloderma.

Dr. Lane replied that three patients so far had died. The patient in the first case reported died of generalized tuberculosis. This was an early case of poikiloderma. Ormsby's patient died of sarcomatosis. The patient in his own case, not yet reported, died a few months ago of Hodgkin's disease. In all reported cases of poikiloderma, the condition grew progressively worse. Few of them had been followed for long, or at least there were few such reports in the literature.

KAPOSI'S SARCOMA. Presented by Dr. Wise for Dr. Fordyce.

I. M., a dentist, aged 45, born in Russia, gave a past history of pneumonia and typhoid fever, but denied venereal disease. The present eruption began four years before, on the hands. Since that time the patient had received forty injections of sodium cacodylate and eight roentgen-ray treatments, with slight improvement, although the disease had continued to spread. Roentgenograms of the lungs had shown areas of calcification suggesting healed tuberculosis. There were two pea-sized violaceous nodules on the left pinna and a quarter-sized linear, violaceous infiltrated lesion on the flexor surface of the right arm. The palm showed violaceous, slightly infiltrated, ill-defined lesions; and on the dorsum of the hand, especially on the knuckles, the lesions were more sharply defined and arranged in plaques giving the appearance of pernio. On the shins were numerous, pea-sized pigmented nodules, and on the outer and inner aspects of both feet there were sharply defined, violaceous scaly and

infiltrated plaques formed by a coalescence of nodules. The patient was under filtered roentgen-ray treatment at the Vanderbilt Clinic, and was receiving sodium cacodylate injections.

DISCUSSION

Dr. Howard Fox asked what treatment the patient had received, and was told that the man had received filtered doses of roentgen rays, which had proved more efficacious than the unfiltered radiation. He said that he had compared the effect of filtered and unfiltered roentgen rays in a case of Kaposi's sarcoma, and he had obtained better results when filtered radiation was used.

PHENOLPHTHALEIN ERUPTION. Presented by Dr. Wise.

G. H., a man, aged 25, single, a teacher, presented a particularly interesting case because he had been taking a cathartic which contained phenolphthalein for one year, without any sign of an eruption, but he did have an eruption after taking other medication. On Aug. 22, 1922, he received an arsphenamin injection for a primary syphilitic sore on the penis. After that he received five arsphenamen injections at five day intervals, intravenously, without any sign of an eruption. The day after the last of these, he was given one mercuric salicylate injection in the buttocks, and the following day the skin presented a typical, generalized phenolphthalein rash, which became more marked after the second injection of mercury. He now presented twenty-five to fifty cent piece sized macules which were brownish and violaceous, scattered over the face, trunk and extremies.

DISCUSSION

The diagnosis was not questioned.

NAEVUS PIGMENTOSUS ET LINEARIS. Presented by Dr. Howard Fox.

M. B. S., a mulatto 11 months of age, born in the United States, presented areas of pigmentation on both buttocks which had been present from birth, and also on the left buttock a linear nevus that had been present, according to the mother's statement, for six months. The pigmented area on the left gluteal region was dark brown, while that on the right side was of a lighter shade. The linear nevus consisted of a patch 4 inches (10.16 cm.) long by one-half inch wide (1.27 cm.), consisting of rough, slightly scaly, pin-head sized papules, which showed some evidence of scratching.

DISCUSSION

The diagnosis was accepted by all.

Dr. Howard Fox called attention to the presence of itching which at first seemed to throw some doubt on the diagnosis of a linear nevus. He had previously, however, treated an adult patient with rather extensive linear nevus who had complained of considerable itching.

PITYRIASIS ROSEA WITH MARKED FACIAL INVOLVEMENT. Presented by Dr. Trimble.

H. W., a girl, aged 14, born in the United States, had had the condition for three weeks. It began on the abdomen. Within a few days after the first appearance of several lesions on the abdomen, the eruption spread rapidly,

involving the arms, back, neck and face. The lesions were about the size of a ten-cent piece, somewhat thickened, scaly and numerous. The condition bore some resemblance to seborrheic eczema, although the foregoing diagnosis was thought to be the correct one.

DISCUSSION

The diagnosis was accepted.

DERMATITIS HERPETIFORMIS. Presented for Dr. Williams by Dr. Traub.

M. C., an Italian woman, aged 22, had been married for two years. During this period she had had two miscarriages, and was three months pregnant when the rash for which she was presented first appeared. Her past history, except for some nervous disorder—either chorea or epilepsy—and mild anemia, was negative. The eruption had existed for eight months, beginning on the hands and arms and spreading shortly to the body and later to the legs. The itching had been intense. At first the rash was papular, but three months ago vesicles and then bullae appeared. The lesions showed a decided tendency to grouping. The healed areas showed a marked pigmentation and some scarring. The active lesions consisted of papules and papulovesicles to small bullae; some of the latter seemed to arise from the normal skin, while others had a decidedly erythematous base. The patient's general health was slightly, if at all, impaired, notwithstanding her statement that she had had a fever reaching 103 F. at irregular periods since the onset of the trouble. The Wassermann test was negative one month before. No biopsy had been made.

SARCOID OF BOECK (MULTIPLE BENIGN MILIARY LUPOID). Presented by Dr. Wise.

J. N., aged 28, a colored woman born in Hayti, married, and a housewife, five years before had been treated at the Vanderbilt Clinic for a seborrheic dermatitis of the scalp and buttocks. The present eruption was of five months' duration and involved her face, chest and elbows. There were numerous pea-sized cutaneous nodules on the backs of her elbows; the skin over these nodules was normal in color. On the mid-sternal region, there was a small atrophic area surrounded by a few violaceous red papules. One violaceous-red, scaly patch, about three-quarters of an inch (1.9 cm.) in size, was located on the bridge of her nose; two patches of similar size and appearance but infiltrated were present on each cheek. Several Wassermann tests were negative, but the microscopic picture of the excised lesion was characteristic.

DISCUSSION

The diagnosis was accepted without dissent.

NEUROTIC EXCORIATIONS. Presented by Dr. Wise. (Previously shown at the Academy of Medicine).

J. I., aged 47, a single man, born in this country, a salesman, had had the condition for fifteen years. The present eruption was of six weeks' duration. On the trunk and extremities, there were numerous brown and pigmented macular lesions. The bearded region showed numerous papulovesicular lesions pinhead to pea sized, some of them indurated. A few papules were present on

the scalp and on the back of the neck. The man had had syphilis eight years before, and had received one course of treatment. He had had several negative Wassermann tests since. He admitted picking at the lesions, and was observed doing so, but Dr. Wise said he was not sure that this was the true explanation for them. A biopsy was not permitted.

DISCUSSION

The diagnosis was accepted.

ADENOMA SEBACEUM. Presented by DR. HIGHMAN for DR. RULISON. (Previously shown in 1922).

After four Kromayer lamp treatments the patient was given compound white lotion in increasing strengths for three months, with improvement. During two months preceding the second presentation, the patient received one-fourth skin unit $\left(\frac{M}{4}\right)$ doses of roentgen rays at weekly intervals. He was shown because of the apparent improvement under roentgen-ray treatment.

DISCUSSION

DR. HOWARD FOX said he believed that the result of the Kromayer light treatment was better than that from electrolysis. The latter method had left some small depigmented scars.

DR. RULISON asked whether any one had had any success in treating such cases with the roentgen ray. He was inclined to believe that the tiny papillomatous growths in this case had decidedly decreased in size since the use of the roentgen ray.

DR. WISE said that Dr. McKee had tried the method, and he said it was not successful.

DR. HIGHMAN referring to the relative benefits of the roentgen-ray and the Kromayer light, said that the latter had unquestionably done more good. Theoretically, he did not understand why the roentgen ray should be of value, and he was inclined to believe that it might be harmful. Nevertheless, if radium could cure, as it did some of the angiomatous types of nevus, there seemed to be no reason why roentgen rays should not be of some benefit in a telangiectatic process which was evidently a congenital anomaly.

ARSPHENAMIN DERMATITIS OF LICHEN PLANUS TYPE. Presented by DR. HIGHMAN.

S. C., aged 27, a clerk, born in the United States, first presented himself for treatment about two years before for an early syphilitic infection, which was treated with arsphenamin and mercury. The specific infection was now four and one-half years old. In May, 1922, a lichenoid eruption developed on the flexor aspect of the arms, appearing as minute papules which did not itch. The eruption had persisted ever since, without disturbing the patient in any way. The case was presented as that type of lichenoid eruption which occurred in connection with arsphenamin therapy, or which might be merely a coincident eruption. The Wassermann test was now negative.

DISCUSSION

DR. WISE said that the diagnosis of lichenoid eruption as a result of arsphenamin treatment seemed the most likely. The condition was not lichen nitidus, for in that dermatosis the color of the papule was the same as the

normal color of the skin in white people. In the negro, it was a little lighter. It greatly resembled a case of lichen planus following the use of arsphenamin, a report of which Dr. McCafferty had recently published.

Dr. Howard Fox agreed with Dr. Wise.

Dr. Whitehouse said that these lichenoid eruptions following arsphenamin medication were unusual.

Dr. Highman said he did not know just how to classify the condition. The eruption appeared after vigorous antisyphilitic treatment. The presence of the eruption was first observed by Dr. Rulison, and since May it had somewhat increased in extent. The patient received his last arsphenamin injection in November, 1922. There was no itching as in lichen planus. Dr. Towle had shown a case at the American Dermatological Association that seemed so typically like lichen planus that those who had not examined it carefully were astonished when the belief was expressed that it was a lichen-like form of arsphenamin dermatitis. Dr. Highman said he had held to his belief that it was lichen planus until Dr. Greenwood of Boston showed him the slides. Later, Dr. Towle had told him that histologically it had proved to be lichen planus. Some of the specimens from Dr. McCafferty's case showed typical lichen planus. Dr. Highman said he had heard of some cases of lichen planus that disappeared under arsphenamin treatment but in general this treatment was not effective. It would not be surprising if now and then lichen planus developed in patients who had received arsphenamin. He was inclined to feel that if arsphenamin were responsible for this picture, it would develop more frequently, considering how often it caused other skin reactions. He did not believe that this was a case of lichen nitidus. Tentatively, and until a histologic study of the case could be made, he would regard it as lichen planus in some way related to arsphenamin, but he could not consider it an example of cause and effect.

PSORIASIS ON PATCHES OF ALOPECIA AREATA. Presented by Dr. Howard Fox.

Dr. Fox reported an unusual condition recently seen in a school girl (E. M.), 12 years of age. She presented typical psoriasis of moderate intensity, situated chiefly on the elbows, knees and scalp, and alopecia areata consisting of three patches varying in size from that of a fifty-cent piece to that of a silver dollar. Both of these diseases had appeared almost simultaneously eleven months previously. The alopecia had disappeared under treatment and had reappeared within the last month. Scattered over the scalp was a moderate number of psoriatic lesions, while on the largest patch of alopecia were situated two typical red and scaly lesions of psoriasis about a quarter of an inch in diameter. This case was recorded on account of the well-known tendency of alopecia areata to be free from any scaling, even when present on a scalp affected by seborrhea or other scaling diseases.

REPORT ON CASE FOR DIAGNOSIS. ULCERS OF THE PENIS. Presented by Dr. Howard Fox. (Previously presented before the New York Dermatological Society on Oct. 24, 1922.)

A. B., an Italian laborer, aged 44, since the last presentation had developed a new ulcer on the penis, similar to the others from which he had suffered. He

was given three injections of neo-arsphenamin, 0.09 gm., at about weekly intervals, beginning December 5, 1922. At the end of three and a half weeks the ulcer had entirely healed, no local treatment being used. Up to Feb. 1, 1923, there had been no new lesions. A histologic examination of a piece of tissue from one of the ulcers excised under local anesthesia was made by Dr. D. L. Satenstein, who reported as follows: "Granuloma. Histological diagnosis not possible. It might well be syphilitic or tuberculous. There is a dilation of the vessels of the upper cutis and a general edema and increase of fibroblasts throughout. The walls of the deeper vessels are hyperplastic. There is a perivascular infiltration composed of plasma epithelioid and round cells and occasional giant cells. New vessels are present, but in no relation to the infiltration. There is no special tubercle formation. The vessel changes suggest syphilis. The cytology of infiltration suggests tuberculosis."

Dr. Highman reported a dermatitis caused by handling English ivy, which he will report in full later.

MINNESOTA DERMATOLOGICAL SOCIETY

Regular Meeting, Feb. 7, 1923

John M. Armstrong, M.D., *Presiding*

LUPUS ERYTHEMATOSUS. Presented by Dr. C. D. Freeman.

Miss S., aged 20, had an eruption which was first noticed on Sept. 15, 1922, consisting of pin-point to lentil-sized bright red papules; some were covered with scales. These lesions were limited to the forehead, cheeks and nose, and were marked on the upper eyelids. There were no subjective symptoms. Her condition was better than at the first appearance. About January 1, similar lesions appeared on the hands and feet.

DISCUSSION

Dr. Butler said he was of the opinion that Dr. Freeman's case was one of the varieties of lupus erythematosus described as the telangiectatic type. He made this diagnosis from the flat erythematous nonscaling patches, which, on close inspection, seemed to be due to new vessel formation.

Dr. Gager said that two years ago last October or November, at one of the meetings, he showed a case of lupus erythematosus of the lower lip involving the mucous membranes, and the diagnosis was concurred in by all members of the Society. He treated the man for a long time under the violet light, also with general radiation. The patient was faithful, and Dr. Gager was able to keep the skin constantly tanned. The lesion healed entirely, and the man has had no recurrence; Dr. Gager suggested the same method of treatment in this case. The lesion itself disappeared in about a year.

CARCINOMA OF THE TONGUE. Presented by Dr. S. Sweitzer.

A man, aged 50, showed a crateriform ulcer on the tip of his tongue. Section showed carcinoma. Three months before, he burned his tongue on a cigaret. The patient was syphilitic.

PSORIASIS OF THE PENIS. Presented by Dr. D. D. Turnacliff.

The patient, aged 30, had on the dorsum of the shaft of the penis, extending back to the pubis, a descrete papular pruritic eruption, coalescing in older areas. Ointments had been used so that all scales were removed, but on the extensor surface of the left forearm there was one papule with an oily scale and pin-point bleeding when the scale was removed. The lesions on the penis had been present for the last year.

DISCUSSION

Dr. Butler said that he disagreed with Dr. Turnacliff's diagnosis of the case. The lesions were, in his opinion, violaceous in color; there was little scaling; the patches were made up of coalesced papules; and the itching was intense. He said that while psoriasis does occasionally itch, this usually occurs in the generalized variety. The patient presented no lesions on the other parts of the body. Dr. Butler believed it was a case of lichen planus.

Dr. Freeman said he believed this was a case of lichen ruber planus.

Dr. Armstrong said he favored a diagnosis of lichen planus.

Dr. Michelson said he favored a diagnosis of psoriasis vulgaris. He said that as the patient had been using an ointment, he would like to see him at the next meeting after he had refrained from using the ointment for one week.

ALOPECIA UNIVERSALIS. Presented by Dr. Michelson.

A boy, aged 11, experienced complete loss of hair of the scalp, eyebrows and eyelids; even the lanugo hairs were not visible. Alpine sun therapy had made no change in the boy's condition. It had been employed for the last five weeks.

DISCUSSION

Dr. Freeman said that he was once interested in a medicolegal case almost similar to the one presented by Dr. Michelson. The patient was working in a factory and was struck by a belt. About two months later, she developed an alopecia universalis. In the testimony, the theory of shock following injury as a probable cause in these cases was advanced and evidently carried considerable weight, as the jury gave the plaintiff a verdict of $2500. About a year later, the patient's brother came to Dr. Freeman with a typical alopecia areata without any history of shock or injury.

ALOPECIA AREATA—CANITIES. DERMATITIS HERPETIFORMIS. Presented by Dr. Michelson.

A man, aged 34, a cook, had been seen at varying intervals for past two years for typical outbursts of dermatitis herpetiformis. At the last attack, five months ago, he had grouped crescentically arranged vesicles which itched intensely, situated in the scapular regions, on the arms, face and scalp. Accompanying this attack, he had alopecia areata. His hair previous to the alopecia was dark brown. It has now returned, but is much more sparse than formerly and snow white.

Dr. Michelson said he thought the case of the man with the dermatitis herpetiformis associated with alopecia areata was of special interest because both of these conditions may be due to some glandular disturbance.

LOCALIZED SCLERODERMA. Presented by DR. TURNACLIFF.

This case had been presented one year ago at the February meeting in St. Paul, at which time the patient had four or five areas from 1 cm. to 5 cm. in diameter, which were glossy white and boardlike with purplish margins. The condition extended up the outer side of the leg, as if following the course of a nerve, to about the height of the greater trochanter of the femur. New lesions formed, and all increased in size and coalesced, forming a large plaque 3 by 8 inches, with several smaller areas above it.

From April to July, the patient received thyroid extract, 1 gm. a day, with no change until September when the lesions spread to their present size. In October, the patient had whooping cough, and when seen again on December 10 the lesions were beginning to involute, until there were only islands of scleroderma scattered through the purplish involuting lesions.

POSTEROSIVE SYPHILOID OF SILVESTER AND JACQUET. Presented by DR. SWEITZER.

A girl, aged 5, presented grouped circinate papules on the buttocks. Some itching was present. The eruption was diagnosed as an inflammatory condition. It was a typical napkin eruption, and had a certain resemblance to a grouped syphilid.

DISCUSSION

DR. MICHELSON said that the dermatitis of Jacquet may be either one of two types: first, an intertrigo type, which usually occurs in ill-kept children; and second, a nodular or urticarial type. This is the type which is most likely to be confused with syphilis. Adamson wrote a splendid article on these conditions some years ago. Both types are resistant to treatment and may last for two or three years.

DR. OLSON said that Leiner described the same condition many years ago, and called it erythema gluteale. The exciting cause is probably the streptococcus.

DR. BUTLER said that this seemed to him like an acute inflammatory condition (diaper dermatitis). There were no nodules that he could see or feel, and the skin showed inflammatory rather than infiltrative changes.

PERIADENITIS MUCOSA RECURRENS NECROTICA. Presented by DR. MICHELSON.

A man, aged 22, a student, said that for last three years he had had recurrent attacks of "sore mouth." He thought they were associated with the state of his digestion.

The mucosa of the lower lip and buccal mucosa were covered with a thin yellowish-white adherent deposit. In the region of the angles of the mouth, there were several jagged, shallow, painful ulcerations. Under potassium chlorate mouthwash, the condition improved greatly, but the patient said this had occurred before only to be followed by a relapse. Diligent search for thrush-fungi and Vincent's organisms proved negative.

DISCUSSION

DR. IRVINE said he thought the question of lupus erythematosus ought to be considered in the question of diagnosis. It is almost impossible to make a

diagnosis of lupus erythematosus limited to the mucous membranes. He said it usually extended over the lips, but he could see no reason why it should not appear on the mucous membranes alone; and this case appeared to him to be like cases of lupus erythematosus when the diagnosis is unquestioned.

DR. SWEITZER said that the condition as diagnosed is supposed to start with a deep-seated nodule that breaks down and ulcerates. He thought the possibility of lupus erythematosus and various fungi would have to be considered.

DR. MICHELSON said that this condition is really a deep-seated chronic aphthous stomatitis. In different diagnosis one must consider: (*a*) Lichen planus. This is ruled out because there were no distinct papules. (*b*) Psoriasis mucosa oris. This is a rare condition and by most authorities is supposed to be a misnomer, for they state that psoriasis is a disease of cornifying cells, and the mucous membrane has no cells which can cornify. (*c*) Leukoplakia was ruled out because of the lack of thickening. (*d*) Lupus erythematosus should involve the vermilion border of the lips, and one should find some cutaneous lesions. All search for causative organisms was negative.

DR. OLSON said that the history and appearance of the lesions pointed to a possible diagnosis of herpes buccalis. He said that herpes buccalis resembled an ordinary herpes simplex, but often was atypical.

TRYCHOPHYTOSIS BARBAE. Presented by DR. BOREEN.

A. T., aged 28, a farmer, referred Dec. 19, 1922, on November 30, while at the soldiers' hospital in St. Paul, noticed a red spot on the right cheek. Two days later it had spread over the whole bearded region. He could not sleep on account of the pain. Examination revealed a swollen face and eyes almost closed. The whole bearded region was covered with pustules, superficial and deep; there were several large plaques sharply marginated and raised. The microscope showed the trychophyton. The case was presented because of its extreme severity and rapid spread. The organism was demonstrated.

A CASE FOR DIAGNOSIS. Presented by DR. KLEIN.

A man, aged 30, had lesions which first appeared on the left buttock five years ago while the patient was working as a cowboy on a ranch. Since then it had spread over the entire buttocks and was rather sharply defined. The border was covered with a heavy scale, and in the center there appeared some crusted areas which occurred on scar tissue. The Wassermann test was negative. At 13 years of age, he had had some glands of the neck incised, which probably were tuberculous. Neo-arsphenamin and mercury did not alter the character of the lesions, and I am inclined to believe that this is a case of lupus, in spite of the rapid development.

DISCUSSION

DR. MICHELSON said he believed this was the most striking case that had been shown before the Society for five years. His diagnosis was lupus vulgaris verrucosus. Against nodular syphilis was the fact that there were numerous lesions recurring within the scar, and in favor of tuberculosis was the fact that the patient had scars on his neck of previous suppurating glands which were operated on, and that the lesions had existed for such a long time with so little ulceration. He also had a fistula-in-ano.

NOTE.—Microscopic section made by Dr. Michelson and reported at next meeting showed typical lupus tubercules.

DR. BUTLER said that Dr. Klein's history of the case threw a new light on the situation. His first diagnosis was lupus vulgaris, but the patient was 30 years of age, and he said it is extremely rare to find lupus vulgaris beginning after the age of puberty. The area of skin involved (all of the buttocks) would require many years if it were lupus. Dr. Butler said he had never heard of lupus vulgaris covering such a large area in five years.

DR. KLEIN said that arsphenamin and mercury given intravenously had had no effect on the lesions except perhaps to make some of the areas become a little more dry; some of the lesions in the center were decidedly crusted, showing that this was an exudative process. The scars on the neck, he thought, were probably from old scrofulodermas and not at all shaped like those found in syphilis. He was inclined to believe that this was a skin tuberculosis—probably of the verrucous type—in spite of the short duration of the process.

DR. IRVINE said he believed it was a fairly good general rule that lupus of the skin starts by the twelfth year. However, he recalled a case shown before the Dermatological Association in Chicago in a man 60 years of age, that was of this same type. Serpiginous lesions occurred in a large area over the chest, and spread rapidly, and in only five or six years they reached a large size. Some of the other members at that meeting also described somewhat similar cases in adult life.

DR. ARMSTRONG said that in his hospital practice several years before arsphenamin treatment became general, he had seen several cases of tubercular syphilis fully as large as this. In one case the whole abdomen and chest were involved. In that case, however, the condition did break down and at the time the patient entered the hospital was infected with maggots.

DR. FREEMAN said he believed this to be a case of lupus vulgaris verrucosus, or tuberculous verrucosus cutis, not syphilis. He said there were a dozen areas of recurrence in scars which is characteristic of lupus vulgaris verrucosus but which is never seen in syphilis.

LICHEN PLANUS WITH A ZOSTER-LIKE DISTRIBUTION. Presented by DR. BUTLER.

The involuting patches showed the distribution of a herpes zoster dorsalis. There was no history of a preceding zoster.

ACRODERMATITIS CHRONICA ATROPHICANS. Presented by DR. MICHELSON.

Both upper and lower extremities were involved in a woman, aged 52. There was no history of preceding scleroderma. Clinically, this was a textbook picture of the condition. Microscopically, section showed extreme thinning and atrophy of the epidermis.

ERYTHRODERMA PITYRIASIQUE EN PLAQUE DISSEMINÉE. Presented by DR. SWEITZER.

Miss M., a woman, aged 68, presented a scaly patchy eruption of sixteen years' duration. Clinically, it looked like mycosis fungoides; the section resembled erythroderma of Brocq.

DISCUSSION

DR. GAGER said he would like to ask why at this stage of the disease, having had it for sixteen years, the woman had not developed tumors. He still thought it was mycosis fungoides.

DR. BUTLER said, with respect to Dr. Gager's statement, that there are four well-defined stages of mycosis fungoides. In the first, or premycotic stage, a biopsy is of no avail, as it shows nothing diagnostic of the disease. The histologic picture is found in the stage of infiltration, or better still in the tumor stage.

DR. MICHELSON said he felt the question was whether or not we were dealing with a case of Brocq's disease. The lesions had been present for a good many years, with no retrogression or further development. Dr. Michelson made a microscopic section that showed almost complete lack of infiltration, the changes being those slight ones which are so commonly associated with Brocq's disease. He thought, nevertheless, that one would have to be guarded in his prognosis.

DR. IRVINE said he thought it difficult to get away from the clinical picture of mycosis fungoides. He could feel these lesions when he passed his finger over them, and he recalled one case in which the areas were large and well marked but could not be felt. There was some infiltration, he said, and it might depend on whether the microscope showed it sufficiently characteristic to make a diagnosis.

ERYTHEMA INDURATUM. Presented by DR. SWEITZER.

Miss F., aged 60, had brown, indurated lesions on the lower part of the legs. Some scarring from older lesions was present. On the toes were small papules, and there was circulatory disturbance.

BASAL-CELL EPITHELIOMA OF THE MORPHEA TYPE. Presented by DR. MICHELSON.

A man, aged 47, a furniture-finisher, said that for the last four years he had had a shallow, progressively enlarging, crusted ulcer situated on his right temple. He had used various ointments. The lesion was about the size of a silver dollar. It had a definite rolled pearly border elevated about 0.5 mm. As the border had advanced, scarring had occurred. Section revealed a typical basal-cell epithelioma. Dr. Michelson intended to treat the patient with radium.

DISCUSSION

DR. ARMSTRONG said that this case corresponded with the one shown by Dr. Sweitzer some time ago, except that in Dr. Sweitzer's case the condition was much more extensive.

KERATOSIS PILARIS. Presented by DR. MICHELSON.

A man, aged 19, had numerous follicularly situated horny plugs situated over the triceps muscle and anterior thigh areas. The case was demonstrated because of the extraordinary extent of the involvement.

The case was of especial interest because the condition had to be differentiated from lichen spinulosus. In this case, the papule with the plug in the center was absent; merely the horny follicular plug was present.

D. D. TURNACLIFF, Secretary.

PHILADELPHIA DERMATOLOGICAL SOCIETY

Regular Meeting, Feb. 12, 1923

F. D. WEIDMAN, M.D., *Presiding*

FRAMBESIFORM SYPHILID. Presented by DR. F. D. WEIDMAN.

E. H., a white man, aged 24, a chauffeur, had had a chancre five months before presentation. He received prompt treatment by mercury injections, but discontinued treatment before completing the course. The Wassermann test was now four plus. The present eruption developed one month ago and consisted of yellowish red patches of superficial infiltration attaining the size of a palm. The margins of the lesions were crusted, not unlike a seborrheic dermatitis, while the center of many showed a soft red "tumor," some of which were superficially ulcerated. They were located mostly on the trunk, although a few smaller ones occurred on the face. The patient had marked epitrochlear and cervical gland enlargement.

DISCUSSION

DR. SCHAMBERG said he belived this type of syphilis was more common since arsphenamin had come into use, because of the usually insufficient treatment. He regarded the condition as a late secondary syphilis due to insufficient treatment.

ADENOMA SEBACEUM. Presented by DR. JOSEPH KLAUDER.

D., a girl, aged 13, presented pinhead sized papules varying in color from yellowish white to brownish red, involving the cheeks and nose. The surface of some of the lesions was vascularized. The patient was subnormal mentally. Her father, who was also shown, also presented lesions of adenoma sebaceum. The same condition was present in his brother, his father and the latter's brother. The females of the family, other than the patient, were unaffected.

DISCUSSION

DR. SCHAMBERG said the condition is quite commonly found in the institutions for mentally defective children.

DR. FREEMAN said that tuberose sclerosis of the brain often is associated with adenoma sebaceum.

ERYTHEMA INDURATUM AND SYPHILIS. Presented by DR. GREENBAUM for DR. SCHAMBERG.

A woman, aged 28, had several ulcerations on the legs, which she said were due to the breaking down of previous lumps. There were numerous scars on the legs, due to the former presence of similar lesions over a period of three or four years, which the patient said developed during the winter months and healed during the summer. When the patient came to the clinic, she had a four plus Wassermann reaction. During the course of neoarsphenamin treatment, the lesion over the left tibia developed, first as a nodule and then as an ulceration, which seemed to indicate definitely that we were dealing with two conditions.

DISCUSSION

Dr. Joseph Klauder said the condition might be a fixed arsphenamin eruption similar to phenolphthalein eruption.

Dr. Weidman asked how one could exclude Bazin's disease.

Dr. Schamberg said it seemed to be a case both of erythema induration (Bazin's disease) and syphilis. Syphilis favors the development of tuberculosis.

MULTIPLE SEBACEOUS CYSTS. Presented by Dr. F. D. Weidman.

F. B., a colored man, aged 40, with advanced pulmonary tuberculosis, had subcutaneous nodules which had been present from twenty to thirty years. In view of an evident phthisis pulmonaris, it was felt that Darier-Roussy sarcoid had to be excluded. Sections were imperfect, but no tuberculous architecture could be made out.

NEUROTIC EXCORIATION. Presented by Dr. Henry Decker.

J. C., a man, aged 65, during June, 1921, while working as a box-maker in a glass factory at Millville, noticed that his face began to itch and burn excessively. He rubbed the areas which itched and noticed that blisters formed, ruptured and became crusted, and when the crusts dropped off or were removed, a scar remained. The condition gradually became worse and involved his pubic region around the site of his truss-pad. This necessitated the discontinuance of wearing the truss and also caused him to stop work. During December, 1922, the patient came to the office. At that time he had several bullae on his neck and forehead with almost symmetrical scarring in front of each ear. Ointment prescribed made the itching worse. A lotion prescribed at a subsequent visit had almost the same effect. During January he was given ⅛ of a skin unit dose of roentgen-ray to both sides of the face and the public region. This controlled the itching for a period of three weeks, and as a result the patient has no new lesions. His Wassermann test was negative. His urine, on one examination, was clear, acid in reaction, with a specific gravity of 1.015, and was negative for albumin and sugar.

DISCUSSION

Dr. Schamberg said he believed this to be a case of erythema bullosum sycosiforme with bleb formation.

WHITE SPOT DISEASE. Presented by Dr. Patricia Hart-Drant.

S. M., a white woman, aged 26, fractured her skull in October, 1921. She recovered and returned to work in February, 1922, and in April she noticed spots in the left inferior clavicular region, which in size and color appeared as discrete silvery scales. In several months these lesions became confluent, extending upward to the supraclavicular region. The area now appeared white and glossy with cross hatching. There was practically no induration. Six months after the appearance of the lesions, pigmentation occurred above the area. Since November the lesions had increased rapidly, appearing on the back, abdomen and over the sternum and thighs. No subjective symptoms preceded the first lesions, but the patient complained of slight itching on undressing, and preceding the appearance of new patches. The medical history was negative. The Wassermann test was negative.

DISCUSSION

Dr. Schamberg said he considered this a borderline case, between a morphea and white spot disease.

Dr. Herschler said he believed it was a case of white spot disease.

Dr. Corson said he believed it looked more like a morphea, the violaceous edge being suggestive.

ONYCHIA SYPHILITICA. Presented by Dr. Greenbaum.

M. B., a woman, aged 38, said that all nails were involved at the same time, about five months before. The nails of seven fingers developed a painful condition at the "overhang," with subsequent ridging and dull appearance of the nails as seen at presentation. There was no history of miscarriages. The patient had been married for three years, and the Wassermann reaction was four plus.

SEBACEOUS ADENOMA. Presented by Dr. C. K. Dengler.

S. F., a boy, aged 9, an epileptic child, whose mental condition was subnormal, had typical lesions of sebaceous adenoma on the cheeks and nose.

FIBROMA MOLLUSCUM. Presented by Dr. Patricia Hart-Drant.

E. C., an Irish girl, aged 26, presented tumors scattered over almost the entire body and associated with pigmentation. She said they had always existed. The tumors were not painful and varied from small superficial, elevated masses, very soft in consistency and covered by apparently normal skin, to more deeply seated tumors which were fairly firm in consistency and vascular. The pigmentations ranged from diffuse freckle-like blotches to patches several inches in diameter. The patient seemed normal mentally. The Wassermann test was negative. Biopsy showed soft fibroma with nerve trunks and some hyaline degeneration.

MYCOSIS FUNGOIDES. Presented by Dr. Weidman.

Sam G., an Italian, 42 years of age, had had the disease for eight years. The same patient was shown before the Society two years ago, with universal reddening and thickening of the skin, palmar keratosis and ungual dystrophy, and a general adenopathy. The inguinal nodes were the largest, then the cervical, axillary and epitrochlear nodes. There had never been any cutaneous infiltrations or tumors up to that time. Itching and chilliness were marked. His white cell count at one time reached 30,000, and the lymphocytes 60 per cent. The number of eosinophils was normal. The liver and spleen were not enlarged. Lymph nodes were excised and a hyperplasia of lymphocytes was found which would not of itself justify a diagnosis of lymphatic leukemia but which excluded Hodgkin's disease. His whole body was fractionally irradiated (seventeen treatments) in two courses, the courses being twenty-one days apart. All this appertains to conditions two years ago. Since that time his blood cell count has dropped, but he has not improved otherwise. After the courses of treatment twenty-three blood counts have been made. The lowest red blood cell count was around 4,000,000; hemoglobin, 62 per cent; but both have averaged well. Before stating the white blood cell findings, a new series of roentgen-ray treatment must be described. This time the cervical and inguinal nodes were

treated; each three times at intervals of three to four weeks. This happened a year ago and consumed five months. His white blood cell findings were: before treatment, 19,300; after the first treatment, 25,600; after four treatments, 7,900. Theafter it has swung consistently around 8,000 (six counts). The differential counts were: before irradiation, 65 to 77 per cent. of lymphocytes; during irradiation, around 45 per cent. of lymphocytes, but falling as low as 13 per cent.; after irradiation, 25 per cent. of lymphocytes, but falling as low as 9 per cent. Eosinophils ranged between 6 and 10 per cent., the number only occasionally being normal. During the last week eczematoid infiltrative patches appeared on the back. They were not like those of parapsoriasis, but appeared edematous and the skin surface was wrinkled. The patient did not feel itchy, but was still chilly; otherwise he felt well.

Review and Summary: The course appeared much like that of leukemia cutis, except that the blood count did not reach the usual levels. Obviously, it could not be quite called an aleukemic leukemia. The recent infiltrations could be conceived just as well of leukemic as of mycosis fungoides production, and up to the time of examination of sections of them the presenter did not feel justified in making a diagnosis. Dr. Schamberg always contended this was a case of lymphatic leukemia.

CASE FOR DIAGNOSIS. Presented by Dr. Patricia Hart-Drant.

P. M., a colored woman, aged 29, presented white circumscribed blotches varying in size from that of a pea to that of half a dollar, occurring on the arms—particularly on the upper arms—and on the thighs. She first noticed these lesions in September, 1922, appearing on the arm as grayish spots which gradually turned white. The skin was smooth with no signs of erythema or scaling. There were no subjective symptoms. The medical history was negative. The Wassermann test and urinalysis were negative. The blood count revealed: leukocytes, 4,800; red blood cells, 4,480; hemoglobin, 85 per cent The differential count: polymorphonuclears, 64 per cent—small, 20 per cent.; large, 16 per cent.

DISCUSSION

Dr. Schamberg said he considered the depigmentation due to a squamous dermatitis, a superficial inflammation resulting in partial loss of pigment.

DERMATITIS FACTITIA. Presented by Dr. Joseph Klauder for Dr. Weidman.

A woman, aged 50, born in America, was a tabetic patient. She had mental symptoms and was probably a taboparetic. She presented sharply circumscribed excoriated lesions, of variable size. The distribuiton was across the upper part of the back and the external surface of both upper extremities. A few lesions were present on the forehead, on the legs and about the center of the lower portion of the back. In some areas, the lesions were grouped, and some were serpiginous in outline. There were also associated scars and pigmented areas which doubtless represented the site of involuted lesions.

DISCUSSION

Dr. Weidman said the lesions suggested prurigo nodularis.

Dr. Greenbaum said that syphilis must be considered as a likely diagnosis.

Dr. Shamberg said it was a classic picture of neurotic excoriation and not a feigned eruption.

MULTIPLE TELANGIECTASIA IN PATCHES (ANGIOMA SERPIGENOSUM?). Presented by DR. F. D. WEIDMAN.

J. W., a white man, 65 years old, had chronic heart disease. He said that the condition did not develop until thirty years before. There were two patches of lesions, each about the size of the palm. The one over the right flank consisted of closely and uniformly-placed telangiectasis of the common cavernous, senile type. Those in the second patch, located over the left side of the abdomen, were mostly made up of fine points recalling cayenne-pepper points; on pressure the red color was largely discharged and a faint brown pigmentation appeared. The points sometimes composed short lines, but none was ever definitely serpiginous or annular. The legs showed varicose veins. There was a patch of solid hyperpigmentation of chronic eczema rubrum on the left leg, and on both legs finely punctate pigmentary marks like those of Schamberg's disease. The patient said the changes in the leg were fourteen years old, that is, subsequent to the abdominal changes. The Wassermann test was negative. The one patch on the abdomen may have the significance of the commonplace senile talangiectasia in an exaggerated form, but not the second; and as it would be illogical to consider the two patches as unrelated, the presenter preferred to interpret them as acquired effects—most likely constitutional, but not necessarily syphilitic, as in Stokes' more extensive case.

NECROPSY FINDINGS IN A CASE OF XANTHOMA TUBEROSUM PREVIOUSLY REPORTED. Presented by DR. WALTER FREEMAN.

The patient was shown at the meeting of Nov. 15, 1921. At that time he presented multiple yellow nodes in the skin over the body and extremities, following especially the distribution of the sebaceous glands, the creases of the palms, and the lips and eyelids. In addition he was greatly jaundiced, had a large hard liver, multiple defects in the skull, and diabetes insipidus. The blood cholesterol was about 400 mg. per 100 c.c.

The boy was not benefited by his stay in the hospital and failed to improve later, although he was able to play about the house. He died rather suddenly about Dec. 1, 1922.

On external examination, only a slight change from the condition present when he was exhibited here was found. The xanthomatous nodules were perhaps somewhat larger in some areas. There was severe jaundice. The gallbladder was filled with clear colorless bile, and the hepatic ducts blocked by a large yellow fibrous mass in the hilum of the liver. There was much adult fibrous tissue with scattered xanthoma cells. There was a considerable increase in the perilobular connective tissue in the liver, with here and there xanthomatous formations. The lungs presented yellow fibers and streaks running in all directions. Histologic examination showed xanthoma cells following the trabeculae, together with some evidences of chronic inflammation. There was no true consolidation. The heart, spleen and kidneys showed no important lesions. The lymph nodes showed characteristics of hemolymphatic alteration. There was a tumor about 12 mm. in dameter in the tuber cinereum extending down the infundibulum into the pituitary gland. The surface was bright yellow, the rest dark green. Under the microscope, there was found much fibrous tissue with xanthoma cells, fat and cholesterin crystals. A similar condition affected the pineal body. The tumors in the skull showed replacement of the normal bone by heavy strands of fibrous tissue interspersed with xanthoma cells, cholesterin clefts and crystals, and foci of lymphocytic infiltration.

DISCUSSION

DR. SCHAMBERG said that both he and Dr. Riesman had shown cases of xanthoma in diabetes.

JOHN B. LUDY, Secretary.

NEW ENGLAND DERMATOLOGICAL SOCIETY

Quarterly Meeting, Feb. 14, 1923

LORETTA JOY CUMMINS, M.D., *Presiding*

FOLLICULITIS ULERYTHEMATOSA RETICULATA. Presented by DR. CASSELBERRY.

A school girl, 11 years old, had an eruption on both cheeks which started when she was 2 or 3 years old. It had continued to spread somewhat. She showed a symmetrical eruption which had the appearance of white raised lines running into each other and forming a network or reticulum. Between these were pinkish depressions with horny plugs of epithelium at their bases. On the cheeks, the reticulum and the plugs were coarser than near the ears and neck. A few milia were seen about the eyes and a few comedones on the reticulated edges. Sulphur and salicylic acid in varying strengths had been used, with the result that many of the horny plugs disappeared and stopped forming. The skin was much softer but the medication did not have much influence on the atrophy or scarring. Suggestions for treatment were requested.

DISCUSSION

DR. BOARDMAN asked whether the Kromayer light would not peel off the eruption a litle.

DR. MACDONALD remarked that he had had good success with a girl who had had a burn with a resulting atrophic scar and a fine raised periphery, which had been trimmed down with trichloracetic acid.

DR. LANE said that he had been interested in trying out trichloracetic acid on the edges of slight depressions similar to the ones seen in this case. He had read of Dr. Wise's results in the treatment of smallpox scars and had immediately painted around the periphery with 100 per cent. trichloracetic acid, then a narrow strip with 50 per cent., and still farther out with 25 per cent., thus beveling it off so that it would not cast so much of a shadow. Careful application would probably reduce the shadows cast in this case.

A CASE FOR DIAGNOSIS. Presented by DR. SAWYER.

A woman, 61 years old, married, the mother of fourteen children, had an eruption which began between the shoulders and persisted for some time, later appearing elsewhere on the body, so that she now showed areas on the back, chest and face. There were a number of rather firm white atrophic areas, rather sharply marked off, in these locations. The itching was intense and worse at night.

DISCUSSION

DR. PERRY remarked that it seemed to him a case of morphea of a rather unusual type.

DR. GREENWOOD said that Dr. Lane and he had recently seen a case which was a picture of this one. At first it had seemed to be a morphea, but they agreed that the presence of those horny plugs indicated a diagnosis of atrophic lichen planus. In addition, in their particular case there were typical papules of lichen planus. The case presented did not show any. He believed it to be an atrophic lichen planus. His patient had received a solution of potassium arsenic (Fowler's solution), and he had used the Alpine lamp, which had resulted in great relief.

DR. BLOSSER remarked that it seemed to him to be a case of scleroderma.

DR. LANE said that he would add a word in regard to Dr. Greenwood's case. He thought that the articles in the literature were quite striking as to the presence of the horny plugs, and the absolute whiteness, with the horny plugs, would make it a case of lichen planus atrophicus rather than scleroderma.

LICHEN PLANUS ATROPHICANS. Presented by DR. LANE.

A Jewish woman, 60 years old, a housewife, had had an eruption for eight months. The areas appeared first on the back and gradually spread over the shoulders and chest, with considerable itching. She presented a great many small white atrophic areas which in places, especially on the chest, coalesced to form larger similar areas. In one place on the epigastrium, also on the arm, there were fairly typical lesions of lichen planus.

LUPUS ERYTHEMATOSUS. Presented by DR. SWARTZ.

A young woman showed lesions on the face of four months' duration and following a sunburn, according to her story. She showed a typical butterfly type of lupus erythematosus on the face, and the case was presented to show the results of treatment. She will be given silver arsphenamin intravenously, because it has been used with success in some cases. The case will be shown again later.

PROBABLE SYPHILITIC ADENITIS. Presented by DR. LLOYD.

A young man came to the outpatient department on January 31 with a lump on the right side of the neck. The tuberculosis clinic failed to find any evidence of tuberculosis, and the throat department stated that while the tonsils were not normal they thought the tonsils were not sufficiently at fault to cause the condition in the neck. The routine Wassermann test was returned as positive. More intensive questioning indicated that his paternal ancestor was at fault. He had received two injections of arsphenamin, resulting in a considerable decrease in the size of the glands.

DISCUSSION

DR. BOARDMAN said that he had a patient who presented marked syphilitic glands which responded quickly at first to treatment, but which finally were reduced to about half the size and remained stationary. The gland finally suppurated and surgical treatment was required.

DR. LLOYD remarked that Dr. Mallory stated that he had never seen what they both believe is syphilitic degeneration of the glands, but they have seen glands which have been enlarged in the late secondary or early tertiary periods and which have yielded to antisyphilitic treatment.

SECONDARY SYPHILIS. Presented by Dr. Lloyd.

A boy, aged 15 years, had secondary syphilis. The port of entry was not clear. He had had a tonsillectomy in July, 1922, at one of the Boston hospitals and he said that he had had a discoloration in the neck for about four months. He also had well marked glands in the neck, which I believe were not the result of degeneration but of infection, and also well marked glands in the axillary and inguinal regions. The pigmentation on the neck and the condition on the trunk interested us particularly. We had recently seen another case in which it was perfectly logical to assume that the infection was in the throat. There was no history of any primary lesion, and yet the cervical adenitis, which was marked, pointed to the throat.

DISCUSSION

Dr. Macdonald cited a case at the Carney Hospital which was almost similar to this—that of a woman aged 36 years, who had had large tonsils, with a positive blood test. Under antisyphilitic treatment the tonsils shrank, and there was almost nothing left of them.

Dr. Spraghe told of a patient who had developed primary lesions and who had been treated outside the hospital, who was also told that he did not need any more treatment until he had a rash. He later had secondary lesions on the tonsils, which were removed. The man came back to the hospital in a unfortunate condition as a result of the operation.

A CASE FOR DIAGNOSIS. Presented by Dr. Macdonald.

A woman, aged 55 years, had had symptoms for five months. The lesion was situated anteriorly and laterally on the tongue at the level of the anterior pillars of the fauces. The lesion was a reddish, papillomatous eruption with no subjective symptoms except a "raw feeling as if the skin was off." It was traversed by numerous small vessels which disappeared posteriorly on the surface of the anterior pillars of the fauces. The patient had had her present tooth-plate for three years. It had never given her any trouble. The Wassermann test was negative. The family history was negative.

DISCUSSION

Dr. Lee remarked that the condition seemed more like hypertrophy of the normal tissue. He said that he did not think that it was distinctively a new growth but rather an inflammatory condition.

Dr. Greenwood said that he agreed. At the Huntington Hospital, during cancer week, they saw many similar cases.

Dr. Blaisdell said he believed that near the junction of the throat and the base of the tongue were several distinctly jelly-like papules suggesting that it was a lymphangioma circumscripta.

Dr. Lloyd remarked that the right side of the tongue seemed normal, the only abnormality noted being a slight increase in the red color about each pillar.

TINEA FAVOSA. Presented by Dr. Swartz.

Four children of one family, all American born, had tinea favosa. The oldest girl being 16 years old, had had the condition for nine years, and she

had gone to school without missing a day. These patients were shown because they had been missed by the school inspectors and because the children are all American born.

ADENOMA SEBACEUM. Presented by DR. CUMMINS.

A woman, 22 years old, had lesions which developed when she was 16 years old, gradually increasing in size and number. She showed a great many small, rounded, yellowish-white and white papules, rather thickly studded over both lower lids. A few were now developing on the upper lid. There was some question whether this was xanthoma or adenoma sebaceum.

DISCUSSION

DR. LANE said that on the same day this girl came into the clinic there was an elderly man there with a definite adenoma sebaceum, and when these two cases were seen together they looked very much alike. He believed this was a case of adenoma sebaceum.

DR. CASSELBERRY said that he believed the location of the lesions was very much against adenoma sebaceum. While he thought they could not be called chamois colored, they were not the slightly pink color seen in adenoma sebaceum. He thought it was more apt to be a xanthoma, although not a particularly marked case.

ALOPECIA AREATA (?) Presented by DR. SWARTZ.

A boy with oval, semibald areas in the occipital region, four years ago had had a similar condition which partially cleared. Last summer there was a recurrence, and he now had fifteen or twenty semibald, smooth areas, without any signs of scaling or redness. He had used no medicine. Cultures were negative.

DISCUSSION

DR. GREENWOOD said he believed the diagnosis was between an alopecia areata and a pseudopelade.

DR. LEE remarked that the amount of scaling seemed to favor an inflamatory condition rather than an ordinary alopecia areata.

EPITHELIOMA OF THE NOSE, SHOWING THE RESULT OF RADIUM TREATMENT. Presented by DR. GREENWOOD.

This man came to the clinic in August, 1922, with the entire tip of the nose eroded, the edges elevated and firm, with considerable crusting. It was apparently a steadily growing basal cell epithelioma. He had been treated with our half strength applicators, used at the first treatment with a 1.2 mm. brass filter, for six hours. On the second treatment, the time was five hours with the same filtration. So far as can be seen the lesion is completely healed.

DISCUSSION

DR. BLAISDELL remarked that it took six or seven different applications, of six hours each to cover the whole nose. It seemed to point out that no matter how large the ulceration or how deep, there is no difficulty in healing a lesion over the bony surface. We never see a chronic ulceration over the bridge of the nose.

DR. LANE remarked that a similar case was under treatment in the roentgen-ray room, in which the lesion was nearly healed. In this case, 12.5 mg. needles, unscreened, had been used rather than the plaques.

SECONDARY SYPHILIS. Presented by DR. LLOYD.

A man, whose lesions have been present for six months, was shown, not on account of the difficulty of diagnosis, but because it is rather unusual to have such marked lesions. He gave a history of infection about six months before. There was a widespread eruption of large flat papules and smaller follicular lesions, often grouped together to form large areas. He had had two injections of arsphenamin, with a fair amount of improvement. It had been rather curious to see the larger flat papules disappear slightly faster than the smaller follicular lesions.

A CASE FOR DIAGNOSIS. Presented by DR. TOWLE.

A blacksmith from Newfoundland entered the ward with two lesions one on each leg, symmetrically placed, surrounded by a fiery red zone, covered with bullae and vesicles. The lesions were quadrilateral and not rounded. The duration of the condition was fifteen months. There was some itching when the lesions first appeared. There had been some question as to whether this was an erythema multiforme.

DISCUSSION

DR. OLIVER said that at the present time the condition looked more like psoriasis or eczema.

DR. MACDONALD said he believed the diagnosis was eczematoid dermatitis.

DR. BLOSSER said that the condition had a distinctly artificial look.

DR. CASSELBERRY said that it was not possible to make a diagnosis at the present time and that he could not see the bullae which were spoken of. He believed it was necessary to be more or less careful when one sees bullae or vesicles on the left side of the body where a person can reach them with the hands.

DR. GREENWOOD said that the psychiatrist had been over this man and that there was nothing in his mental condition to warrant a diagnosis of fictitious dermatitis. There was no history of taking drugs internally.

A CASE FOR DIAGNOSIS. Presented by DR. TOWLE.

The fourth and fifth in a series of seven children were presented for diagnosis. The mother had had no miscarriages, and there had been no still-births. The last child died at the age of 9 months from pneumonia, with a questionable patch of similar nature on one cheek. The skin lesions appeared at about the age of 9 or 10 months in the younger and at 3 years of age in the older, the faces and hands being involved at the same time, with the condition slowly progressing. Ectropion had been present in the older for only about 2 months. The condition was always worse during the summer. Both children had lateral pendulum nystagmus. The urine was negative for hematoporphyrin and the Wassermann and Pirquet tests were negative. Their foreheads, cheeks, the backs of both hands and also forearms were covered with a thin, atrophic, rough, slightly pigmented skin. These areas faded gradually into the surrounding skin.

DISCUSSION

DR. LANE remarked that he saw these children when they first came in and he thought that the actinic element was in some way responsible for the condition. There were certain areas on the side of the forehead in the older child in which the atrophy suggested a lupus erythematosus, but the distribution of the rest of the lesions on the areas exposed most to sunlight, was much more in favor of the condition being due to some actinic element. He believed that the condition should be placed in the xeroderma pigmentosa group, perhaps the erythematous stage.

DR. LEE said he believed that the whole picture indicated a scleroderma.

DR. PERRY said he also believed the condition was scleroderma.

CONGENITAL SYPHILIS AND PSORIASIS. Presented by DR. LLOYD.

A young woman with congenital syphilis presented herself about six months ago. She received numerous injections of arsphenamin and improved to a certain degree. She had had a rest period, and the arsphenamin treatment was started again four weeks before, and after she had received two injections she began to have a much roughened skin which looked like the beginning of arsenical dermatitis. It proved, however, to be a definite, generalized, acute type of psoriasis.

DISCUSSION

DR. LANE told of a recent similar acute psoriasis which had cleared up under generalized ultraviolet light treatment.

DR. MACDONALD told of similar cases treated with ultraviolet light at the Carney Hospital.

LATE SYPHILIS. Presented by DR. SWARTZ.

A married woman, 23 years old, with one child living and well, who had had no miscarriages, began to have chapped lips, which gradually grew worse and spread to the chin, about six months ago. There was definite thickening of the lip. Redness extended down on the skin, and there were a few irregular macular lesions on the chest. The Wassermann test was strongly positive.

DISCUSSION

DR. LLOYD remarked that this case was a practical example of the type in which there is a full amount of interstitial thickening right in the muscular tissue of the lip.

ST. LOUIS DERMATOLOGICAL SOCIETY

Regular Meeting, Feb. 14, 1923

RICHARD S. WEISS, M.D., *Presiding*

A CASE OF LICHEN PLANUS HYPERTROPHICUS. Presented by DR. RICHARD KRING.

A. K., aged 18, gave a history of having had typhoid fever in September, 1919, at the age of 15. He was confined to his bed for six weeks, and then developed phlebitis, his legs being swollen from the foot to the knee. In

November, 1920, he had an eruption on both legs, with large, pustular lesions and some destruction of the tissue. He now has infiltrated plaques of various size on the right leg, covered with dense adherent scales; some of the lesions are circinate. There is the same type of lesion on the left leg, also several lesions on the buccal surface. His father and mother are living. The patient has had the usual diseases of childhood; he has had no venereal disease. The Wassermann test and urinalysis were negative.

DISCUSSION

Dr. R. H. Davis said that he supposed all present had arrived at the diagnosis in this case, observing the hypertrophic condition presented. He stated that in his opinion it was undoubtedly hypertrophic lichen planus. All present concurred in this opinion.

EPIDERMOMYCOSIS OF THE HANDS. Presented by Dr. A. H. Conrad.

A man, aged 44, a clinic attendant and "first-aid worker," had an eruption on both hands. He had had a similar attack in August, 1922, when he was seen by Dr. Weiss during Dr. Conrad's absence. At that time, he also had large vesicles on his feet. The lesions on his hands lasted about six weeks. The present trouble began February 5, with a large number of small vesicles between the fingers and a few in the palms of the hands. Three days after, the entire surface of the hands became involved. He now presents a large number of small vesicles with a crusting of the first and second fingers of the right hand and an exfoliation of the palms of the hands. When Dr. Conrad saw him on February 8, after applying a modified Whitfield salve, he came back in two days and showed great improvement in the lesions between the fingers and palms, but the lesions were very much more numerous on the back of the left hand. The case was presented on account of the rapid spread of the condition in contradistinction to the great majority of cases in which the lesions remain in their respective location for a great length of time.

DISCUSSION

Dr. McIntosh said that he believed it was a case of pompholyx.

Dr. R. H. Davis said that perhaps it was a case of epidermophytosis.

Dr. Brockelmann said that he believed it might be a trade dermatitis.

Dr. Kring concurred in his opinion.

Dr. Greiner diagnosed the condition as pompholyx.

Dr. Weiss concurred. He said that when he saw the patient last summer, he called the condition an epidermophyton infection. Now, however, as the eruption had come on so suddenly, with acute edema of the hands and fingers and with deep-seated vesicles in the palms and vesicles over the backs of the hands, it seemed to him that it should be called pompholyx. He said he had seen a number of patients with these cases who recovered quickly on a non-protein diet., and that Dr. Engman had had the same experience.

Dr. Conrad said he was of the opinion that it was a mycotic infection as the lesions were typical, being between the fingers. When he first saw the patient, the lesions on the left hand were superficial, not as deep-seated as in cheiropompholyx. He called attention to the rapid spreading of the eruption.

The patient improved very much under treatment for a mycotic condition, which was a modified Whitfield salve, after which he returned in a few days, showing great improvement. If the condition were cheiropompholyx, the treatment would not have been as effective. Dr. Conrad said this was the reason that he considered mycosis, the patient having had previous attacks, one on the hands and one on the feet.

Dr. Weiss said that he believed that the disease which we have been calling "pompholyx" really belonged to the erythema group. The symptoms seem to be caused by an intestinal protein poisoning. By removing the protein products from the intestinal tract, the source of the poisoning is removed, and the patient improves. There have been a number of cases cited in these meetings in which an attack of pompholyx could be provoked by a large protein meal. Then, in the natural course of events, by discontinuing the protein or by diminishing it, the source of the poisoning would disappear from the intestinal tract, and the patient would soon show improvement. The effect of medicine on the skin in this type of disease should be discounted, for the mere fact that a person improves is not an evidence per se that the salve has been the curative agent.

Dr. R. H. Davis remarked that it is true that we have epidermophyton cases that arise quite suddenly and which are as suddenly cured.

Dr. Weiss agreed that he had seen a number of such cases.

Dr. Conrad said that the reason he had counted on the diagnosis of epidermophyton was because of the superficial condition of the vesicles. He said that in cheiropompholyx they are underneath the deeper structures and not superficial, and that close observation of the lesions under discussion—especially that on the back of the left hand—shows that they are superficial.

A CASE OF RECURRENT LUPUS ERYTHEMATOSUS AFTER SEEMINGLY COMPLETE RECOVERY FOLLOWING AN ATTACK OF TYPHOID FEVER. Presented by Dr. A. H. Conrad.

A woman, aged 23, a billing machine operator, whose family history was negative, except that her uncle had tuberculosis, had had the usual diseases of childhood and typhoid fever in 1918, the illness lasting three months. The present trouble consisted of an eruption on the nose which began about eight years before as a small bite on the back of the neck. This spread over the entire back of the neck up to the hairline, the lesion attaining a size of 4 inches (10.16 cm.) in diameter. This remained for about one year. About three months after the lesion had made its appearance on the back of the neck, the patient noticed a similar lesion on the forehead just above the nose. This then spread down on the nose and on both cheeks on a line with the wing of the nose. At this time the patient was seen by one of our physicians who made a diagnosis of lupus erythematosus. Carbon dioxid was used, with some good results. After a slight reaction, following the application of the carbon dioxid, which caused the face to swell, the patient became alarmed and discontinued treatment. After the lesion had been on the face for about two years, she contracted typhoid fever. She was very ill, having a high temperature, and was in bed for three months. During the latter part of her illness, the lesion became much smaller. During her convalescence, the lesion disappeared entirely. The patient said that there was no eruption on her face from early in 1919 to the latter part of 1920, at which time the lesion again became

apparent at the present site, and it has remained practically the same size for the last one and a half years. She now presents an area about 1½ inches (3.81 cm.) in diameter on the bridge of the nose, which is rough in appearance and touch, somewhat infiltrated, and dark reddish-purple. On the left cheek near the nostril is some scarring, which was the site of a former lesion.

DISCUSSION

DR. WEISS said that the fact that a lupus erythematosus disappears under parenteral protein treatment was well demonstrated by Drs. Engman and McGarry, when cases of long standing cleared up after injections of typhoid vaccine. Many of them recurred. This case cleared up on autogenous typhoid organisms and a recurrence was to be expected.

DR. CONRAD remarked that the patient gave a history of having had lesions on the back of the neck. He said he did not believe that this was a lupus erythematosus, but something entirely different. The lesion at the present site has been there for a long time, an indefinite period, but it seemed to him that it did not grow any larger, was not very deep, but rather superficial in comparison to some that he had seen. He asked the opinion of those present in regard to treatment of such a lesion with acetic acid.

DR. WEISS replied that he had tried a few cases with some success on a mixture of equal parts of phenol and lactic acid, as suggested by some one in the *British Journal of Dermatology* a few years ago. He said he believed that the roentgen ray and radium offer the best chance of recovery, although with a small lesion, carbon dioxid might bring good results.

DR. R. H. DAVIS said that he had also used carbon dioxid with benefit.

DR. CONRAD said that Dr. Mook had used carbon dioxid on two or three occasions, followed by a severe reaction causing swelling of the face, which so alarmed the mother of the patient that she discontinued the use of the carbon dioxid.

DR. R. H. DAVIS remarked that in the use of carbon dioxid near the eyes, unusual swelling was likely to occur.

A CASE FOR DIAGNOSIS. Presented by DR. RICHARD KRING.

H. C., a woman, aged 20, single, engaged in housework, had an eruption on the forearms and backs of the hands. The patient's father was living; the mother died of cerebral hemorrhages. The patient had had the usual diseases of childhood, several attacks of tonsillitis, also attacks of appendicitis and pneumonia. Urinalysis was negative; the Wassermann test was negative. The present condition had existed about one year. The eruption was itchy at night. It was in the form of minute papules, polygonal in shape, with shiny tops, and flat. The lesions on the arms were crusted, papular—of the same type as the lesions on the legs. There were no lesions in the mouth.

DISCUSSION

DR. GREINER said that when he saw the case some months before, the lesions on both forearms and limbs were typical of a lichen planus. It appeared to him that the lesions had been undergoing a change, that the case was now resulting in psoriasis, at least that is what it appeared to be. He remarked that he had never before seen lesions undergo such a change as in this case.

DR. CONRAD said that on close inspection it was seen that some of the lesions were almost typical of lichen planus, although the aspect of the case in its entirety was that of psoriasis.

DR. R. H. DAVIS said that he had seen some cases some years ago which, like this case, had appeared to be lichen planus at first and had passed through successive periods, at one time looking like lichen planus, and then again like psoriasis, and ending in an "erythrodermie pityriasique en plaques disseminées."

DR. WEISS said he believed that it was a typical psoriasis, judging from the appearance of the lesions on the limbs.

DR. KRING said that this case in the beginning looked like lichen planus, having undergone a marked change.

A CASE FOR DIAGNOSIS. Presented by DR. RICHARD KRING.

Mrs. T., aged 55, a widow, engaged in housework, complained of itching ankles, which she scratched. A vesicular and pustular eruption then developed; also several ulcers on both legs. The skin was red; there were some crusting and scaling. On both popliteal spaces there were dry, somewhat large scaly patches which were itchy; they were spreading gradually and had a sharp line of demarcation on the border. The ulcers on the limbs had healed, leaving scars. There was mild ichthyosis of the skin. The urinalysis and Wassermann test were negative.

DISCUSSION

DR. GREINER remarked that he had no comment to make other than to say that he had watched the case from time to time for about three months. The patient seemed to be improving gradually. She had come under observation about a year before, and had been a patient in the clinic for about a month. Then she disappeared and did not return until about a month ago, at which time she was very much worse than when presented.

DR. R. H. DAVIS said that the condition looked like a neurodermatitis, but that he merely mentioned this as a suggestion and would like to know the method of treatment in this case.

DR. GREINER replied that the patient had had no internal medication—merely local treatment.

DR. WEISS observed that one might guess at the course of events in this case. The patient had had some lesions which healed, leaving scars in some instances. The scars interfered with the return flow of the circulation. There was mild edema of the limbs in proportion to the scarring, and hence lowered resistance of the skin. Then there were itching and scratching and therefore traumatic dermatitis. As a result of the injury due to itching and scratching, various salves were applied, some probably irritating, and as a further result of the scratching and application of the salve, there would naturally be an increase of eczema due to the extreme rubbing. The final result would be lichenification, which is what the patient's condition looked like to him.

DR. CONRAD said that he did not agree with Dr. Weiss. If the patient's ankles were observed, raised dark red lesions could be seen, not entirely to be accounted for by the explanation given.

DR. WEISS then referred to a case presented at the previous meeting showing a more or less similar condition, which Dr. Engman included in his classi-

fication of eczematoid dermatitis. Follicular infection and constant irritation will produce a peculiar raised border in such cases. Dr. Engman had recommended an application of 5 per cent. pulverized rhubarb in petrolatum, rhubarb containing a small percentage of chrysarobin which is helpful in such conditions.

Dr. R. H. Davis said that he believed Dr. Weiss' suggestion an ingenious one, probably accounting for a good deal of the skin condition, although there were some points about it which were puzzling. One point was the almost perfect symmetrical distribution which could not be accounted for by the scratching. He said that in his experience, these symmetrical distributions had either an arteriosclerotic or a neurotic basis. The arteriosclerotic type was usually found in old people, and ended in a sharp line below the knees. This woman had a peculiar symmetry, not like that resulting from itching and scratching. Dr. Davis said he thought that there was in this case a neurotic basis.

Dr. Greiner said that he would like to add that the patient had a mild ichthyosis. She had also had an attack of double phlebitis in both limbs, with chills and fever and high temperature.

Dr. Weiss remarked that under those circumstances, the condition of edema and symmetry could be explained.

Dr. Kring remarked also that the patient was very neurotic, and that he thought neurosis had something to do with it.

A CASE FOR DIAGNOSIS. Presented by Dr. Richard Kring.

Mrs. C., aged 50, married, was presented on account of lesions on the eyelids, which began at the age of 17 and continued to grow. The patient had had seven children, four of whom are living. Menstruation began at the age of 12; menopause occurred at 40. The patient had backaches and rheumatism, neuritis in the right knee and pyorrhea. The pains disappeared on removal of the teeth. She was also operated on for hernia. The patient's general health was good. The lesions on the eyelids were chamois colored, soft to the touch, irregular in shape, and were distributed on both upper and lower lids. Urinalysis was negative as to sugar and albumin; the Wassermann test was negative. (The patient said that her daughter, 17 years of age, had one small lesion on one of her eyes.)

DISCUSSION

Dr. Kring suggested xanthoma palpebrarum as a diagnosis, which was accepted without further discussion.

A CASE OF RECURRENT PITYRIASIS ROSEA (?). Presented by Dr. A. H. Conrad from Dr. Engman's Clinic at Washington University.

This patient was presented at the previous meeting of the St. Louis Dermatological Society because of a profuse papular eruption. The consensus of opinion was that it was a case of pityriasis rosea—Dr. Grindon dissenting. The child had steadily improved up to about twelve days before, when there were only a few stains and excoriations left. Ten days before, he began to break out again, and he again had a more or less generalized crop of papular lesions, from 3 to 5 mm. in diameter, yellowish-red, with slightly scaly tops, and raised 1 or 2 mm. above the surface, sparsely scattered on the posterior

aspect of the trunk, more thickly on the anterior aspect, and thickly on the neck, with a few on the face. The soles were free. There were scattered papules in the palms, rather deep but not of the same color.

DISCUSSION

Dr. Greiner said that after hearing the history of the case and seeing the lesions, he believed it dermatitis herpetiformis.

Dr. Kring said that he had not thought of dermatitis herpetiformis, as this is usually associated with a good deal of itching, the formation of vesicles and sometimes pustules and small crusts—but that he would not venture a diagnosis.

Dr. Tobias said that it looked to him like a dermatitis from some obscure cause that could perhaps be tested with proteins.

Dr. Weiss remarked that it was peculiar that the lesions had left pigmentation. When he first saw the patient, he was of the opinion that the condition was pityriasis rosea, but he could not find any typical plaques. With the present recurrence a number of plaques were seen that were more or less typical, and in addition there were several lesions on the palms—which was not unknown in pityriasis rosea. He believed that if it were a pityriasis rosea, it was at least a second attack, instances of this sort being found in the literature. One instance was reported in a discussion on pityriasis rosea in the proceedings of the American Dermatological Association, 1913, Dr. Dyer reporting that he himself had had an attack of pityriasis rosea after taking a Turkish bath, and that some weeks later, on revisiting the Turkish bath, he had another attack. Dr. Weiss concluded that the case under discussion was a recurrent attack of pityriasis rosea with unusual features.

Dr. Conrad remarked that it seemed to him like a possible recurrent attack, some plaques being typical of pityriasis rosea, the only puzzling feature being the discoloration or pigmentation which some of the lesions had left.

A CASE OF DIFFUSE SCLERODERMA (SCLERODACTYLIA TYPE). Presented by Dr. Norman Tobias.

J. S., aged 37, married, born in the United States, said that the condition began in 1917 as a numbness, followed by a thinning of the skin of the fingers, and about one year later by stiffness, pigmentation and glossiness of the wrists and contracture of the fingers with pigmentation of the neck. The toes and feet also became involved at this time, but to a lesser extent. The condition soon affected her mouth, which appeared smaller and stiff; her lips thinned; her nose shrunk in size, and the lobules of her ears became atrophic. In 1918, she entered the Barnes Hospital and remained there for six weeks; she received "hip injections" and a biopsy was made. Since then, her condition had gradually extended to its present degree. Physical examination revealed a generalized scleroderma of the hands, forearms and face especially, with a mild involvement of the neck and lower extremities. There was a characteristic pinched expression of the face and a lack of expression in speaking. Deep fossae were present in the submaxillary regions (tonsillectomy was performed at the age of 13, in 1918, at the Barnes Hospital). The right lobe of the thyroid gland had been enlarged since adolescence. The chest showed pigmentation and telangiectasia. The abdomen was pigmented, there was a thick abdominal wall. The thighs were well developed. The reflexes were negative. The blood pressure was: systolic 80, diastolic 62; urinalysis and the Wassermann test were negative.

DISCUSSION

Dr. Tobias said that this patient did not remain long enough under treatment to have any blood or urine tests made, but, as Dr. Weiss had suggested, he had attempted to find arsenic in the urine, as reported in the literature on the subject. If arsenic can be found in the urine later, sodium hyposulphite will be administered as a therapeutic measure. Roentgenograms of the hands will be presented at the next meeting of the Society.

A CASE OF POSSIBLE SUPERINFECTION. Presented by Dr. A. H. Conrad from Dr. Engman's Clinic at Washington University.

A colored man, aged 45, a laborer, applied to the Medical Clinic on Oct. 29, 1922, complaining of a pain in the left breast. The diagnosis at that time was aortitis, aneurysm in the arch of the aorta. The patient gave a history of having had a chancre fifteen years before; there was no history of an eruption. The Wassermann test was ++++ on Oct. 27, 1922. He was immediately put on a course of intramuscular injections of 15 minims of mercuric chlorid and potassium iodid. He received twenty-two of these injections given at intervals of three days. Two days after the last injection, January 31, he received 0.05 gm. arsphenamin. On January 28, he had an itching sensation at the site of the present lesion, with a slight excoriation. This continued to grow larger, and now was about 1 cm. by 8 mm., was roughly oval in shape, and somewhat indurated. The lesion was covered with a dirty, grayish discharge, and the left inguinal gland was somewhat enlarged. Dark-field examination of the spirochetes was negative.

VIENNA DERMATOLOGICAL SOCIETY

Session of June 22, 1922

Dr. Oppenheim, *In the Chair*

DISSEMINATED PUSTULAR LICHEN SCROFULOSORUM. Presented by Dr. Kren.

The eruptions along the back and the nates first suggested pustular syphilis. The pustules were partly grouped and based on a nodular infiltration. The Wassermann reaction was negative; the Pirquet and intracutaneous reactions with old tuberculin were positive.

TOXICODERMA DUE TO INDIAN HEMP. Dr. Porias.

Cannabis indica contains an alkaloid cannabin and resin. Either of these can cause a toxicoderma. In the case presented, the patient, who had been handling hemp, developed an erythroderma over the face and scalp. Removal of the causative factor affected a rapid regression of symptoms.

ERYTHRODERMA SOLARE ON AN EXTENSIVE VITILIGO OF THE SCALP. Dr. Porias.

The erythema showed a sharp margin against the pigmented skin of the face. Small patches of vitiligo within the unaffected part of the face also showed small angiectiases and erythematous alterations.

ARSPHENAMIN DERMATITIS WITH DAMAGE TO THE CORNEA. Dr. Kumer.

In a patient who had received 8 injections of neo-arsphenamin, a dermatitis developed simultaneously with a keratitis superficialis punctata of the left eye. The latter developed into an ulcer, with subsequent cicatrization.

ATYPICAL SCROFULODERMA FOLLOWING THE INJECTION OF A NEW TUBERCLE BACILLI EMULSION. Dr. Arzt.

At the site of injection, nodules developed which had a tendency to break down and discharge a puslike secretion. Histologic examination revealed a chronic inflammatory process, the nodules containing epithelioid and giant cells. The picture very much resembled that of scrofuloderma.

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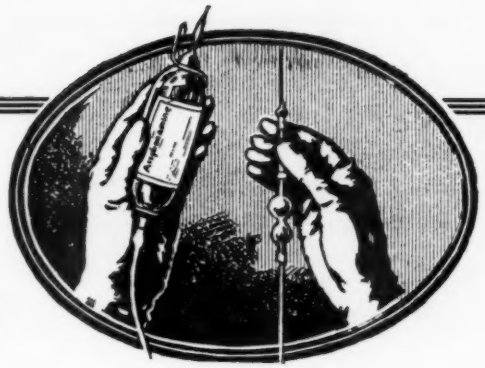

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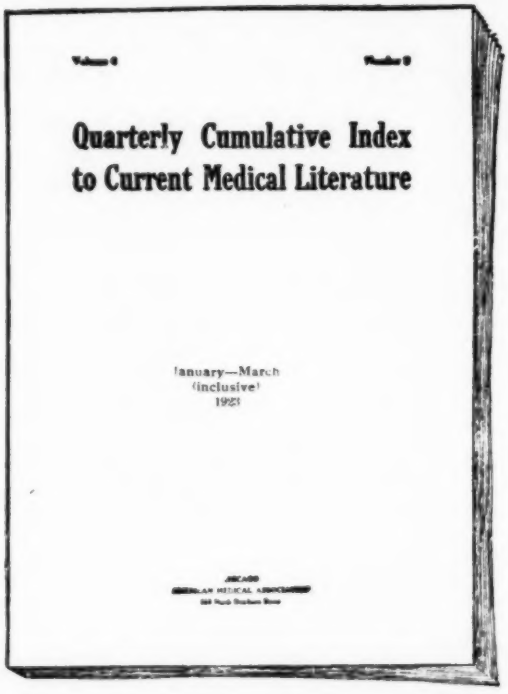

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